

# Arterial Hypertension

< Introduction >

< What is new and what has changed? >

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Introduction



New evidence has emerged since the 2013 [ESH/ESC](#) Arterial Hypertension Guidelines and this has resulted in changes to some of the recommendations in the 2018 [ESC/ESH](#) Hypertension Guidelines which are highlighted in [Table 3](#). In addition, the new guidelines contain a number of new sections, recommendations and concepts, as shown in [Table 4](#).



## Table 4 New sections, recommendations and concepts

### New sections/recommendations

- When to suspect and how to screen for the causes of secondary hypertension
- Management of hypertension emergencies
- Updated recommendations on the management of [BP](#) in acute stroke
- Updated recommendations on the management of hypertension in women and pregnancy
- Hypertension in different ethnic groups
- The effects of altitude on [BP](#)
- Hypertension and chronic obstructive pulmonary disease
- Hypertension and AF and other arrhythmias
- Oral anticoagulant use in hypertension
- Hypertension and sexual dysfunction
- Hypertension and cancer therapies
- Perioperative management of hypertension
- Glucose-lowering drugs and [BP](#)
- Updated recommendations on [CV](#) risk assessment and management: (i) using the [SCORE](#) system to assess risk in patients without CVD; (ii) the importance of [HMOD](#) in modifying [CV](#) risk; and (iii) the use of statins and aspirin for [CVD](#) prevention

### New concepts



## New concepts

### **BP measurement**

- **Wider use of out-of-office BP measurement with ABPM and/or HBPM, especially HBPM**, as an option to confirm the diagnosis of hypertension, detect white-coat and masked hypertension, and monitor BP control.

### **Less conservative treatment of BP in older and very old patients**

- **Lower BP thresholds and treatment targets for older patients**, with emphasis on considerations of biological rather than chronological age (i.e. the importance of frailty, independence, and the tolerability of treatment).
- Recommendation that **treatment should never be denied or withdrawn on the basis of age**, provided that treatment is tolerated.

### **A SPC treatment strategy to improve BP control**

- **Preferred use of two-drug combination** therapy for the initial treatment of most people with hypertension.
- **A single-pill treatment strategy for hypertension**, with the preferred use SPC therapy for most patients.
- **Simplified drug-treatment algorithms** with the preferred use of an ACE-inhibitor or ARB, combined with a CCB or/and a thiazide/thiazide-like diuretic, as the core treatment strategy for most patients, with beta-blockers used for specific indications.

### **New target ranges for BP in treated patients**

- **Target BP ranges for treated patients** to better identify the recommended BP target and **lower safety boundaries for treated BP**, according to a patient's age and specific comorbidities.

### **Detecting poor adherence to drug therapy**

- A strong emphasis on the **importance of evaluating treatment adherence** as a major cause of poor BP control.

### **A key role for nurses, pharmacists in the longer-term management of hypertension**

- **The important role of nurses and pharmacists** in the education, support, and follow-up of treated hypertensive patients is emphasized as part of the overall strategy to improve BP control.

The relationship between [BP](#) and [CV](#) and renal events and mortality is continuous, making the distinction between normotension and hypertension somewhat arbitrary. In practice, threshold [BP](#) values are used for pragmatic reasons, to simplify the diagnosis and decisions about treatment. Hypertension is defined as the level of [BP](#) at which the benefits of, unequivocally outweigh the risks of treatment, as documented by clinical trials.

The classification of [BP](#) and definition of hypertension based on seated office [BP](#) measurement is unchanged from the previous guideline (**Table 5**). Hypertension is defined as office systolic [BP](#) (SBP) values  $\geq 140$  mmHg and/or diastolic [BP](#) (DBP) values  $\geq 90$  mmHg.

**Table 5 Classification of Blood Pressure and definitions of hypertension grade<sup>b</sup>**

Category <sup>a</sup>	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	$\geq 180$	and/or	$\geq 110$
Isolated systolic hypertension <sup>b</sup>	$\geq 140$	and	<90

<sup>a</sup>[BP](#) category is defined according to seated clinic [BP](#) and by the highest level of [BP](#), whether systolic or diastolic.

<sup>b</sup>Isolated systolic hypertension is graded 1, 2, or 3 according to [SBP](#) values in the ranges indicated.

The same classification is used for all ages from 16 years.

## Classification of blood pressure

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
It is recommended that <a href="#">BP</a> be classified as optimal, normal, high-normal, or grades 1–3 hypertension, according to office <a href="#">BP</a> .	I	C

<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.



## < Assessment of CVD risk

Hypertension often clusters with other [CV](#) risk factors such as dyslipidaemia and glucose intolerance, which have a multiplicative effect on [CV](#) risk. Quantification of total [CV](#) risk is important for the risk stratification of patients with hypertension, to determine whether additional treatments such as statins and anti-platelet therapies may be indicated to further reduce [CV](#) risk (see section [here](#)). Classification of [CV](#) risk according to the [SCORE](#) system is recommended (**Table 6**).

Hypertension and cardiovascular risk assessment		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<a href="#">CV</a> risk assessment with the <a href="#">SCORE</a> system is recommended for hypertensive patients who are not already at high or very high risk due to established <a href="#">CVD</a> , renal disease, or diabetes, a markedly elevated single risk factor (e.g. cholesterol), or hypertensive <a href="#">LVH</a> .	I	B

CVD = cardiovascular disease; LVH = left ventricular hypertrophy; SCORE = Systematic COronary Risk Evaluation. <sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.

**Table 6** Ten year cardiovascular risk categories (Systematic COronary Risk Evaluation system)

Very high-risk	<p><b>People with any of the following:</b></p> <p><b>Documented <a href="#">CVD</a>, either clinical or unequivocal on imaging.</b></p> <ul style="list-style-type: none"><li>• <b>Clinical <a href="#">CVD</a></b> includes; acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularization, stroke, <a href="#">TIA</a>, aortic aneurysm, and <a href="#">PAD</a>.</li><li>• <b>Unequivocal documented <a href="#">CVD</a> on imaging</b> includes: significant plaque (i.e. <math>\geq 50\%</math> stenosis) on angiography or ultrasound. It does not include increase in carotid intima-media thickness.</li><li>• <b>Diabetes mellitus with target organ damage</b>, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia</li><li>• <b>Severe <a href="#">CKD</a></b> (<a href="#">eGFR</a> <math>&lt; 30</math> mL/min/1.73 m<sup>2</sup>)</li><li>• <b>A calculated 10-year <a href="#">SCORE</a> of <math>\geq 10\%</math></b></li></ul>
High-risk	<p><b>People with any of the following:</b></p> <ul style="list-style-type: none"><li>• <b>Marked elevation of a single risk factor</b>, particularly cholesterol <math>&gt; 8</math> mmol/L (<math>&gt; 310</math> mg/dL) e.g. familial hypercholesterolaemia, grade 3 hypertension (<a href="#">BP</a> <math>\geq 180/110</math> mmHg)</li><li>• <b>Most other people with diabetes mellitus</b> (except some young people with type 1 diabetes mellitus and without major risk factors, that may be moderate risk)</li></ul> <p><b>Hypertensive <a href="#">LVH</a></b></p> <p><b>Moderate <a href="#">CKD</a> <a href="#">eGFR</a> 30–59 mL/min/1.73 m<sup>2</sup>)</b></p> <p><b>A calculated 10-year <a href="#">SCORE</a> of 5–10%</b></p>
Moderate-risk	<p><b>People with:</b></p> <ul style="list-style-type: none"><li>• <b>A calculated 10-year <a href="#">SCORE</a> of <math>\geq 1\%</math> to <math>&lt; 5\%</math></b></li><li>• <b>Grade 2 hypertension</b></li><li>• <b>Many middle-aged people belong to this category</b></li></ul>
Low-risk	<p><b>People with:</b></p> <ul style="list-style-type: none"><li>• <b>A calculated 10-year <a href="#">SCORE</a> of <math>&lt; 1\%</math></b></li></ul>

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; LVH = left ventricular hypertrophy; TIA = transient ischaemic attack; PAD = peripheral artery disease; SCORE = Systematic COronary Risk Estimation.

Patients with hypertension may also present with features of hypertension-mediated organ damage (HMOD) (see **Tables 13-16**) as well as diabetes mellitus or chronic kidney disease, which may shift the estimated risk according to [SCORE](#) to a higher category as illustrated in **Figure 1**.



< Assessment of CVD risk

Very high-risk	<div>tion, stroke, <a href="#">TIA</a>, aortic aneurysm, and <a href="#">PAD</a>.</div> <ul style="list-style-type: none"><li>• <b>Unequivocal documented <a href="#">CVD</a> on imaging</b> includes: significant plaque (i.e. ≥50% stenosis) on angiography or ultrasound. It does not include increase in carotid intima-media thickness.</li><li>• <b>Diabetes mellitus with target organ damage</b>, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia</li><li>• <b>Severe <a href="#">CKD</a></b> (<a href="#">eGFR</a> &lt;30 mL/min/1.73 m<sup>2</sup>)</li><li>• <b>A calculated 10-year <a href="#">SCORE</a> of ≥10%</b></li></ul>
High-risk	<div>People with any of the following:</div> <ul style="list-style-type: none"><li>• <b>Marked elevation of a single risk factor</b>, particularly cholesterol &gt;8 mmol/L (&gt;310 mg/dL) e.g. familial hypercholesterolaemia, grade 3 hypertension (<a href="#">BP</a> ≥180/110 mmHg)</li><li>• <b>Most other people with diabetes mellitus</b> (except some young people with type 1 diabetes mellitus and without major risk factors, that may be moderate risk)</li></ul> <div>Hypertensive <a href="#">LVH</a></div> <div>Moderate <a href="#">CKD</a> <a href="#">eGFR</a> 30–59 mL/min/1.73 m<sup>2</sup>)</div> <div>A calculated 10-year <a href="#">SCORE</a> of 5–10%</div>
Moderate-risk	<div>People with:</div> <ul style="list-style-type: none"><li>• A calculated 10-year <a href="#">SCORE</a> of ≥1% to &lt;5%</li><li>• Grade 2 hypertension</li><li>• Many middle-aged people belong to this category</li></ul>
Low-risk	<div>People with:</div> <ul style="list-style-type: none"><li>• A calculated 10-year <a href="#">SCORE</a> of &lt;1%</li></ul>

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; LVH = left ventricular hypertrophy; TIA = transient ischaemic attack; PAD = peripheral artery disease; SCORE = Systematic COronary Risk Estimation.

Patients with hypertension may also present with features of hypertension-mediated organ damage (HMOD) (see **Tables 13-16**) as well as diabetes mellitus or chronic kidney disease, which may shift the estimated risk according to [SCORE](#) to a higher category as illustrated in **Figure 1**.

**Figure 1 Classification of hypertension stages according to blood pressure levels, presence of cardiovascular risk factors, hypertension-mediated organ damage, or comorbidities**

Hypertension disease staging	Other risk factors, HMOD, or disease	BP (mmHg) grading			
		High normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP 160-179 DBP 100-109	Grade 3 SBP ≥180 or DBP ≥110
Stage 1 (uncomplicated)	No other risk factors	Low-risk	Low-risk	Moderate risk	High-risk
	1 or 2 risk factors	Low-risk	Moderate risk	Moderate to high-risk	High-risk
	≥3 risk factors	Low to Moderate risk	Moderate to high-risk	High-Risk	High-risk
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high-risk	High-risk	High-risk	High to very high-risk
Stage 3 (established disease)	Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high-risk	Very high-risk	Very high-risk	Very high-risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; HMOD = hypertension-mediated organ damage; SBP = systolic blood pressure; SCORE = Systematic COronary Risk Evaluation.

<sup>a</sup>[CV](#) risk is illustrated for a middle-aged male. The [CV](#) risk does not necessarily correspond to the actual risk at different ages. The use of the [SCORE](#) system is recommended for formal estimation of [CV](#) risk for treatment decisions.



**BP** may be measured in the doctor's office, at home or by ambulatory **BP** monitoring (ABPM). In all cases, it is important that **BP** is measured carefully using a validated device (**Table 7**).

### Table 7 Office blood pressure measurement

Patients should be seated comfortably in a quiet environment for 5 min before beginning **BP** measurements.

Three **BP** measurements should be recorded, 1–2 min apart, and additional measurements only if the first two readings differ by >10 mmHg. **BP** is recorded as the average of the last two **BP** readings.

Additional measurements may have to be performed in patients with unstable **BP** values due to arrhythmias, such as in patents with AF, in whom manual auscultatory methods should be used as most automated devices have not been validated for **BP** measurement in patients with AF.<sup>a</sup>

Use a standard bladder cuff (12–13 cm wide and 35 cm long) for most patients, but have larger and smaller cuffs available for larger (arm circumference >32 cm) and thinner arms, respectively.

The cuff should be positioned at the level of the heart, with the back and arm supported to avoid muscle contraction and isometric exercise-dependant increases in **BP**.

When using auscultatory methods, use phase I and V (sudden reduction/disappearance) Korotkoff sounds to identify **SBP** and **DBP**, respectively.

Measure **BP** in both arms at the first visit to detect possible between-arm differences. Use the arm with the higher value as the reference.

Measure **BP** 1 minute and 3 min after standing from seated position in all patients at the first measurement to exclude orthostatic hypotension. Lying and standing **BP** measurements should also be considered in subsequent visits in older people, people with diabetes, and people with other conditions in which orthostatic hypotension may frequently occur.

Record heart rate and use pulse palpation to exclude arrhythmia.

AF = atrial fibrillation; BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.

<sup>a</sup>Most automatic devices are not validated for **BP** measurement in patients with AF, and will record the highest individual systolic pressure wave form rather than an average of several cardiac cycles. This will lead to overestimation of **BP**.

Home BP is measured as the average of all BP readings performed with a semiautomatic, validated BP monitor, for at least 3 days and preferably for 6–7 consecutive days before each clinic visit, with readings in the morning and the evening, taken in a quiet room, after 5 min of rest, with the patient seated with their back and arm supported. Two measurements should be taken at each measurement session, performed 1–2 min apart.



[ABPM](#) provides the average of [BP](#) readings over a defined period, usually 24 hrs. The device is typically programmed to record [BP](#) at 15–30 min intervals, and average [BP](#) values are usually provided for daytime, night-time, and 24 hrs. A minimum of 70% usable [BP](#) recordings are required for a valid [ABPM](#) measurement session. Home and [ABPM](#) values are on average lower than office [BP](#) values, and the corresponding diagnostic thresholds for hypertension are shown in **Table 8**.

Table 8 Definitions of hypertension according to office, ambulatory, and home blood pressure levels			
Category	<a href="#">SBP</a> (mmHg)		<a href="#">DBP</a> (mmHg)
Office <a href="#">BP</a> <sup>a</sup>	≥140	and/or	≥90
Ambulatory <a href="#">BP</a>			
Daytime (or awake) mean	≥135	and/or	≥85
Night-time (or asleep) mean	≥120	and/or	≥70
24-h mean	≥130	and/or	≥80
Home <a href="#">BP</a> mean	≥135	and/or	≥85

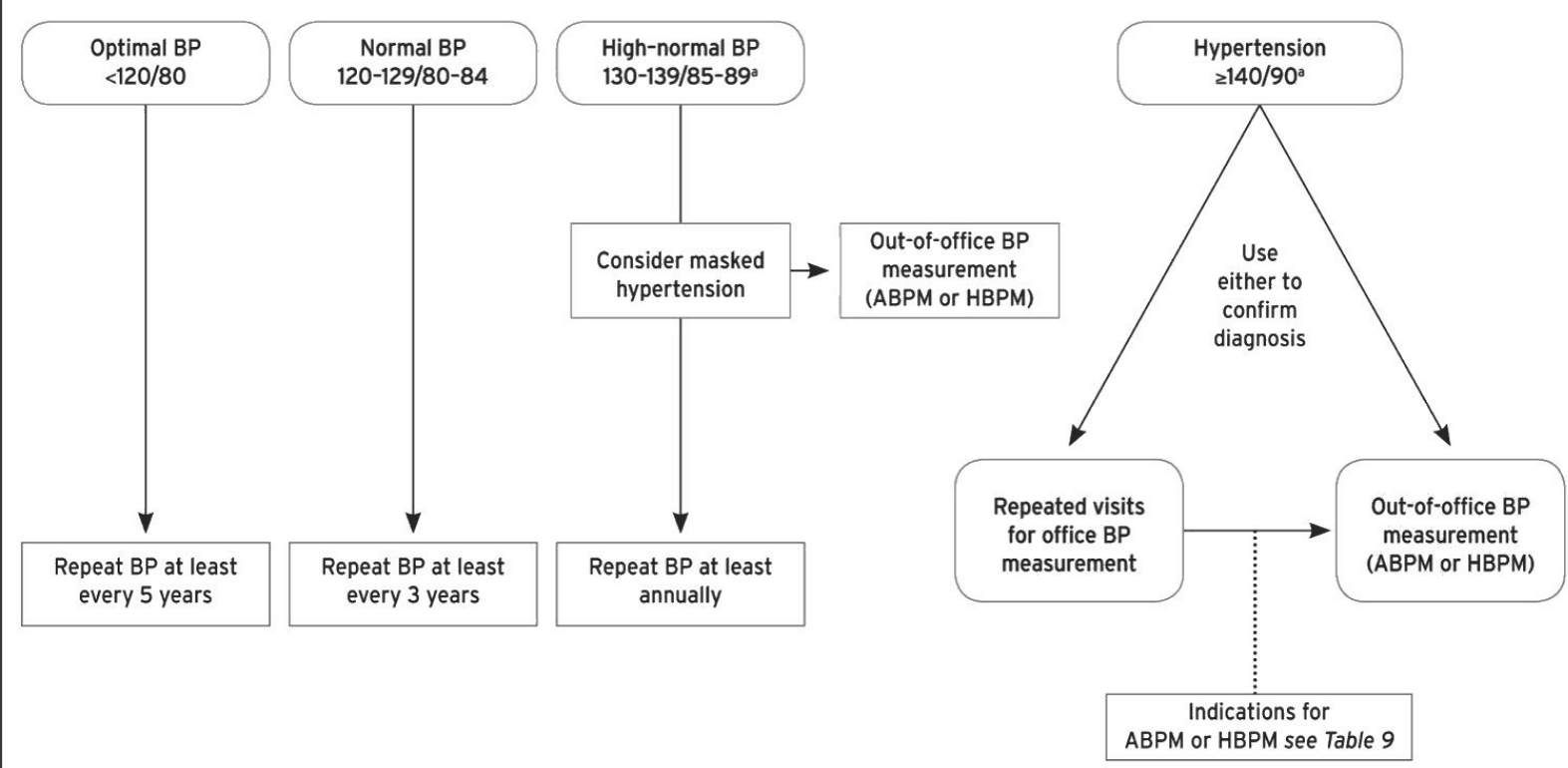
BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.  
<sup>a</sup>Refers to conventional office [BP](#) rather than unattended office [BP](#).

Hypertension is predominantly an asymptomatic condition that is best detected by population screening programmes or opportunistic BP measurement (see **Figure 2**). All adults should have their BP recorded in their medical record and be aware of their BP, and further screening should be undertaken at regular intervals with the frequency dependent on the BP level.

For healthy people with an optimal office BP (<120/80 mmHg), BP should be re-measured at least every 5 years and more frequently when opportunities arise. In patients with a normal BP (120–129/80–84), BP should be re-measured at least every 3 years.

Patients with high-normal BP (130–139/85–89 mmHg) should have their BP recorded annually because of the high rates of progression of high-normal BP to hypertension.

**Figure 2 Screening and diagnosis of hypertension**



ABPM = ambulatory blood pressure monitoring; BP = blood pressure; HBPM = home blood pressure monitoring.

<sup>a</sup>After detecting a specific BP category on screening, either confirm BP elevation with repeated office BP measurements on repeat visits, or arrange use of out-of-office BP to confirm the diagnosis of hypertension.



The diagnosis of hypertension should not be based on a single set of [BP](#) readings at a single office visit, unless the [BP](#) is substantially increased (e.g. grade 3 hypertension) and there is clear evidence of [HMOD](#) (e.g. hypertensive retinopathy with exudates and haemorrhages, or [LVH](#), or vascular or renal damage). For all others (i.e. almost all patients), the diagnosis of hypertension should be based on [BP](#) measurements at repeat office visits, or home [BP](#) or [ABPM](#), when these measurements are feasible ([Figure 2](#)). [ABPM](#) is also indicated for specific indications see **Table 9**.

**Table 9 Clinical indications for home blood pressure monitoring or ambulatory blood pressure monitoring**

Conditions in which white-coat hypertension is more common, e.g. <ul style="list-style-type: none"><li>• Grade I hypertension on office <a href="#">BP</a> measurement</li><li>• Marked office <a href="#">BP</a> elevation without <a href="#">HMOD</a></li></ul>
Conditions in which masked hypertension is more common, e.g. <ul style="list-style-type: none"><li>• High-normal office <a href="#">BP</a></li><li>• Normal office <a href="#">BP</a> in individuals with <a href="#">HMOD</a> or at high total <a href="#">CV</a> risk</li></ul>
Postural and post-prandial hypotension in untreated and treated patients
Evaluation of resistant hypertension
Evaluation of <a href="#">BP</a> control, especially in treated higher-risk patients
Exaggerated <a href="#">BP</a> response to exercise
When there is considerable variability in the office <a href="#">BP</a>
Evaluating symptoms consistent with hypotension during treatment
Specific indications for <a href="#">ABPM</a> rather than HBPM: <ul style="list-style-type: none"><li>• Assessment of nocturnal <a href="#">BP</a> values and dipping status (e.g. suspicion of nocturnal hypertension, such as in sleep apnoea, <a href="#">CKD</a>, diabetes, endocrine hypertension, or autonomic dysfunction)</li></ul>

ABPM = ambulatory blood pressure monitoring; BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; HBPM = home blood pressure monitoring.

Blood pressure measurement		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Screening programmes for hypertension are recommended. All adults (18 years or older) should have their office <a href="#">BP</a> measured and recorded in their medical file and be aware of their <a href="#">BP</a> .	I	B
<ul style="list-style-type: none"><li>• Further <a href="#">BP</a> recording is indicated, at least every 5 years if <a href="#">BP</a> remains optimal.</li><li>• Further <a href="#">BP</a> recording is indicated, at least every 3 years if <a href="#">BP</a> remains normal.</li><li>• If <a href="#">BP</a> remains high-normal, further <a href="#">BP</a> recording, at least annually, is recommended.</li><li>• In older patients (&gt;50 years), more frequent screening of office <a href="#">BP</a> should be considered for each <a href="#">BP</a> category because of the steeper rise in <a href="#">SBP</a> with ageing.</li></ul>	I	C
	I	C
	I	C
	IIa	C
It is recommended that office <a href="#">BP</a> should be measured in both arms at least at the first visit because a between-arm <a href="#">SBP</a> difference of >15 mmHg is suggestive of atheromatous disease and is associated with an increased <a href="#">CV</a> risk.	I	A



< Confirming the diagnosis of HTN

rise in <a href="#">SBP</a> with ageing.		
It is recommended that office <a href="#">BP</a> should be measured in both arms at least at the first visit because a between-arm <a href="#">SBP</a> difference of >15 mmHg is suggestive of atheromatous disease and is associated with an increased <a href="#">CV</a> risk.	I	A
If a between-arm difference in <a href="#">BP</a> is recorded, then it is recommended that all subsequent <a href="#">BP</a> readings use the arm with the higher <a href="#">BP</a> reading.	I	C
It is recommended to base the diagnosis of hypertension on: <ul style="list-style-type: none"><li>Repeated office <a href="#">BP</a> measurements on more than one visit, except when hypertension is severe (e.g. grade 3 and especially in high-risk patients). At each visit, three <a href="#">BP</a> measurements should be recorded, 1–2 min apart, and additional measurements should be performed if the first two readings differ by &gt;10 mmHg. The patient's <a href="#">BP</a> is the average of the last two <a href="#">BP</a> readings.</li></ul> Or <ul style="list-style-type: none"><li>Out-of-office <a href="#">BP</a> measurement with <a href="#">ABPM</a> and/or <a href="#">HBPM</a>, provided that these measurements are logistically and economically feasible.</li></ul>	I	C
Out-of-office <a href="#">BP</a> (i.e. <a href="#">ABPM</a> or <a href="#">HBPM</a> ) is specifically recommended for a number of clinical indications, such as identifying white-coat and masked hypertension, quantifying the effects of treatment, and identifying possible causes of side-effects (e.g. symptomatic hypotension).	I	A
It is recommended that all hypertensive patients undergo pulse palpation at rest to determine heart rate and search for arrhythmias such as AF.	I	C
Other <a href="#">BP</a> measures and indices (pulse pressure, <a href="#">BP</a> variability, exercise <a href="#">BP</a> , and central BP) may be considered but are not often used for routine clinical use at present. They may provide useful additional information in some circumstances and are valuable tools for research.	IIb	C

ABPM = ambulatory blood pressure monitoring; AF = atrial fibrillation; BP = blood pressure; CV = cardiovascular; HBPM = home blood pressure monitoring; SBP = systolic blood pressure.  
<sup>a</sup>Class of recommendation.  
<sup>b</sup>Level of evidence.



# Key info to be collected

The purpose of the clinical evaluation is to:

1. Establish the diagnosis and grade of hypertension.
2. Screen for potential secondary causes of hypertension.
3. Identify factors potentially contributing to the development of hypertension (lifestyle, concomitant medications, or family history).
4. Identify concomitant [CV](#) risk factors (including lifestyle and family history).
5. Identify concomitant diseases.
6. Establish whether there is evidence of [HMOD](#) or existing [CV](#), cerebrovascular, or renal disease.

## Table 10 Key information to be collected in personal and family medical history

### Risk factors

Family and personal history of hypertension, [CVD](#), stroke, or renal disease

Family and personal history of associated risk factors (e.g. familial hypercholesterolaemia)

Smoking history

Dietary history and salt intake

Alcohol consumption

Lack of physical exercise/sedentary lifestyle

History of erectile dysfunction

Sleep history, snoring, sleep apnoea (information also from partner)

Previous hypertension in pregnancy/pre-eclampsia

### History and symptoms of [HMOD](#), [CVD](#), stroke, and renal disease

Brain and eyes: headache, vertigo, syncope, impaired vision, [TIA](#), sensory or motor deficit, stroke, carotid revascularization, cognitive impairment, or dementia (in the elderly)

Heart: chest pain, shortness of breath, oedema, myocardial infarction, coronary revascularization, syncope, history of palpitations, arrhythmias (especially AF), heart failure

Kidney: thirst, polyuria, nocturia, haematuria, urinary tract infections

Peripheral arteries: cold extremities, intermittent claudication, pain-free walking distance, pain at rest, peripheral revascularization

Patient or family history of [CKD](#) (e.g. polycystic kidney disease)

### History of possible secondary hypertension

Young onset of grade 2 or 3 hypertension (<40 years), or sudden development of hypertension or rapidly worsening [BP](#) in older patients

History of renal/urinary tract disease

Recreational drug/substance abuse/concurrent therapies: corticosteroids, nasal vasoconstrictor, chemotherapy, yohimbine, liquorice

Repetitive episodes of sweating, headache, anxiety, or palpitations, suggestive of Pheochromocytoma

History of spontaneous or diuretic-provoked hypokalaemia, episodes of muscle weakness, and tetany (hyperaldosteronism)

Symptoms suggestive of thyroid disease or hyperparathyroidism

History of or current pregnancy and oral contraceptive use

History of sleep apnoea

### Antihypertensive drug treatment

Current/past antihypertensive medication including effectiveness and intolerance to previous medications

Adherence to therapy

AF = atrial fibrillation; BP = blood pressure; CKD = chronic kidney disease; CVD = cardiovascular disease; HMOD =hypertension-mediated organ damage; TIA = transient ischaemic attack.



## Table 11 Key steps in physical examination

### Body habitus

Weight and height measured on a calibrated scale, with calculation of [BMI](#)

Waist circumference

### Signs of hypertension-mediated organ damage

Neurological examination and cognitive status

Fundoscopy examination for hypertensive retinopathy

Palpation and auscultation of heart and carotid arteries

Palpation of peripheral arteries

Comparison of [BP](#) in both arms (at least once)

### Secondary hypertension

Skin inspection – café-au-lait patches of neurofibromatosis (phaeochromocytoma)

Kidney palpation for signs of renal enlargement in polycystic kidney disease

Auscultation of heart and renal arteries for murmurs or bruits indicative of aortic coarctation or renovascular hypertension

Comparison of radial with femoral pulse – to detect radio-femoral delay in aortic coarctation

Signs of Cushing's disease or acromegaly

Signs of thyroid disease

BMI = body mass index; BP = blood pressure; HMOD = hypertension-mediated organ damage.



## Table 12 Routine work-up for evaluation of hypertensive patients

### Routine laboratory tests

Haemoglobin and/or haematocrit

Fasting blood glucose and glycated [HbA1c](#)

Blood lipids: total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol

Blood triglycerides

Blood potassium and sodium

Blood uric acid

Blood creatinine and [eGFR](#)

Blood liver function tests

Urine analysis: microscopic examination; urinary protein by dipstick test or, ideally, albumin:creatinine ratio

12-lead [ECG](#)

eGFR = estimated glomerular filtration rate; ECG = electrocardiogram; HbA1c = haemoglobin A1c.



Table 13 Assessment of Hypertension-mediated organ damage	
Basic screening tests for <a href="#">HMOD</a>	Indication and interpretation
12-lead <a href="#">ECG</a>	Screen for <a href="#">LVH</a> and other possible cardiac abnormalities and to document heart rate and cardiac rhythm
Urine albumin:creatinine ratio	To detect elevations in albumin excretion indicative of possible renal disease
Blood creatinine and <a href="#">eGFR</a>	To detect possible renal disease
Fundoscopy	To detect hypertensive retinopathy, especially in patients with grade 2 or 3 hypertension
More detailed screening for <a href="#">HMOD</a>	Indication and interpretation
Echocardiography	To evaluate cardiac structure and function, when this information will influence treatment decisions
Carotid ultrasound	To determine the presence of carotid plaque or stenosis, particularly in patients with cerebrovascular disease or vascular disease elsewhere
Abdominal ultrasound and Doppler studies	<ul style="list-style-type: none"><li>• To evaluate renal size and structure (e.g. scarring) and exclude renal tract obstruction as possible underlying causes of <a href="#">CKD</a> and hypertension</li><li>• Evaluate abdominal aorta for evidence of aneurysmal dilatation and vascular disease</li><li>• Examine adrenal glands for evidence of adenoma or pheochromocytoma (<a href="#">CT</a> or <a href="#">MRI</a> preferred for detailed examination) – see section <a href="#">here</a> regarding screening for secondary hypertension.</li><li>• Renal artery Doppler studies to screen for the presence of renovascular disease, especially in the presence of asymmetric renal size</li></ul>
PWV	An index of aortic stiffness and underlying arteriosclerosis
ABI	Screen for evidence of <a href="#">LEAD</a>
Cognitive function testing	To evaluate cognition in patients with symptoms suggestive of cognitive impairment
Brain imaging	To evaluate the presence of ischaemic or haemorrhagic brain injury, especially in patients with a history of cerebrovascular disease or cognitive decline

ABI = ankle–brachial index; ABPM = ambulatory blood pressure monitoring; BP = blood pressure; CKD = chronic kidney disease; CT = computed tomography; ECG = electrocardiogram; HBPM = home blood pressure monitoring; HMOD = hypertension-mediated organ damage; LEAD = lower extremity artery disease; LVH = left ventricular hypertrophy; MRI = magnetic resonance imaging; PAD = peripheral artery disease; PWV = pulse wave velocity.



**Table 14 The most commonly used simple criteria and recognised cut-off points for definitions of electrocardiogram left ventricular hypertrophy**

<b><u>ECG</u> voltage criteria</b>	<b>Criteria for <u>LVH</u></b>
$S_{V1} + R_{V5}$ (Sokolow-Lyon criterion)	>35 mm
R wave in aVL	≥11 mm
$S_{V3} + R_{aVL}$ (Cornell voltage) <sup>a</sup> Cornell duration product <sup>b</sup>	>28 mm (men)
	>20 mm (women)
	>2440 mm.ms

ECG = electrocardiogram; LVH = left ventricular hypertrophy.  
<sup>a</sup>Sum of limb and precordial lead voltage - <sup>b</sup>Product of Cornell voltage x QRS duration (mm.ms).

**Table 15 Echocardiographic definitions of left ventricular hypertrophy, concentric geometry, left ventricular chamber size, and left atrial dilatation**

Parameter	Measure	Abnormality threshold
LVH	<u>LV</u> mass/height <sup>2.7</sup> (g/m <sup>2.7</sup> )	>50 (men) >47 (women)
LVH <sup>a</sup>	<u>LV</u> mass/ <u>BSA</u> (g/m <sup>2</sup> )	>115 (men) >95 (women)
<u>LV</u> concentric geometry	RWT	≥0.43
<u>LV</u> chamber size	<u>LV</u> end-diastolic diameter/height (cm/m)	>3.4 (men) >3.3 (women)
Left atrial size (elliptical)	Left atrial volume/height <sup>2</sup> (mL/m <sup>2</sup> )	>18.5 (men) >16.5 (women)

BSA = body surface area; LV = left ventricular; LVH = left ventricular hypertrophy; RWT = relative wall thickness.

<sup>a</sup>BSA normalization may be used in normal weight patients.



**Table 16 Sensitivity to detect treatment-induced changes, reproducibility and operator independence, time to changes, and prognostic value of changes provided by markers of hypertension-mediated organ damage**

Marker of HMOD	Sensitivity to changes	Reproducibility and operator independence	Time to changes	Prognostic value of the change
LVH by ECG	Low	High	Moderate (>6 months)	Yes
LVH by echocardiogram	Moderate	Moderate	Moderate (>6 months)	Yes
LVH by CMR	High	High	Moderate (>6 months)	No data
eGFR	Moderate	High	Very slow (years)	Yes
Urinary protein excretion	High	Moderate	Fast (weeks to months)	Moderate
Carotid IMT	Very low	Low	Slow (>12 months)	No
PWV	High	Low	Fast (weeks to months)	Limited data
Ankle-brachial index	Low	Moderate	Slow (>12 months)	Moderate

CMR = cardiac magnetic resonance; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HMOD = hypertension-mediated organ damage; IMT = intima-media thickness; LVH = left ventricular hypertrophy; PWV = pulse wave velocity.



Clinical evaluation & HMOD assessment		
Clinical evaluation and hypertension-mediated organ damage assessment		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Heart</b>		
12-lead <a href="#">ECG</a> is recommended for all hypertensive patients.	I	B
Echocardiography: <ul style="list-style-type: none"> <li>Is recommended in hypertensive patients when there are <a href="#">ECG</a> abnormalities or signs or symptoms of <a href="#">LV</a> dysfunction.</li> <li>May be considered when the detection of <a href="#">LVH</a> may influence treatment decisions.</li> </ul>	I	B
	IIb	B
<b>Blood vessels</b>		
<ul style="list-style-type: none"> <li>Ultrasound examination of the carotid arteries:</li> <li>May be considered for the detection of asymptomatic atherosclerotic plaques or carotid stenosis, in patients with documented vascular disease elsewhere.</li> </ul>	I	B
	IIb	B
Measurement of <a href="#">PWV</a> may be considered for measuring arterial stiffness.	IIb	B
Measurement of <a href="#">ABI</a> may be considered for the detection of advanced <a href="#">LEAD</a> .	IIb	B
<b>Kidney</b>		
Measurement of serum creatinine and <a href="#">eGFR</a> is recommended in all hypertensive patients.	I	B
Measurement of urine albumin:creatinine ratio is recommended in all hypertensive patients.	I	B
Renal ultrasound and Doppler examination should be considered in patients with impaired renal function, albuminuria, or for suspected secondary hypertension.	IIa	C
<b>Fundoscopy</b>		
Is recommended in patients with grades 2 or 3 hypertension and all hypertensive patients with diabetes.	I	C
May be considered in other hypertensive patients.	IIb	C
<b>Brain</b>		
In hypertensive patients with neurological symptoms and/or cognitive decline, brain <a href="#">MRI</a> or <a href="#">CT</a> should be considered for detecting brain infarctions, microbleeds, and white matter lesions.	IIa	B
ABI = ankle–brachial index; CT = computed tomography; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HMOD = hypertension-mediated organ damage; LEAD = lower extremity arterial disease; LV = left ventricular; LVH = left ventricular hypertrophy; MRI = magnetic resonance imaging; PWV = pulse wave velocity; TIA = transient ischaemic attack. <sup>a</sup> Class of recommendation - <sup>b</sup> Level of evidence.		



Most patients with hypertension will be managed in the primary care setting. There are, however, circumstances in which a referral for hospital-based evaluation and treatment may be required:

- Patients in whom secondary hypertension is suspected.
- Younger patients (<40 years) with grade 2 or more severe hypertension in whom secondary hypertension should be excluded.
- Patients with treatment-resistant hypertension.
- Patients in whom more detailed assessment of HMOD would influence treatment decisions.
- Patients with sudden onset of hypertension when BP has previously been normal.
- Other clinical circumstances in which the referring doctor feels more specialist evaluation is required.

There are also rarer circumstances in which a patient with hypertension should be referred to hospital for emergency care, which will often require in-patient care (see section here).



The routine treatment of hypertension involves lifestyle interventions for all patients (including those with high normal BP) and drug therapy for most patients.

Key considerations are:

- At what BP threshold BP is drug treatment indicated or should be considered?
- How low BP should be lowered?
- What lifestyle and drug treatment strategies should be used to lower BP?



# < BP thresholds for treatment

Lifestyle interventions (see section [here](#)) are recommended for all patients with high-normal [BP](#) or hypertension. The [BP](#) threshold for drug treatment and timing of initiation of drug treatment depends on the patient's age and risk (Figure 3 and Table 17).

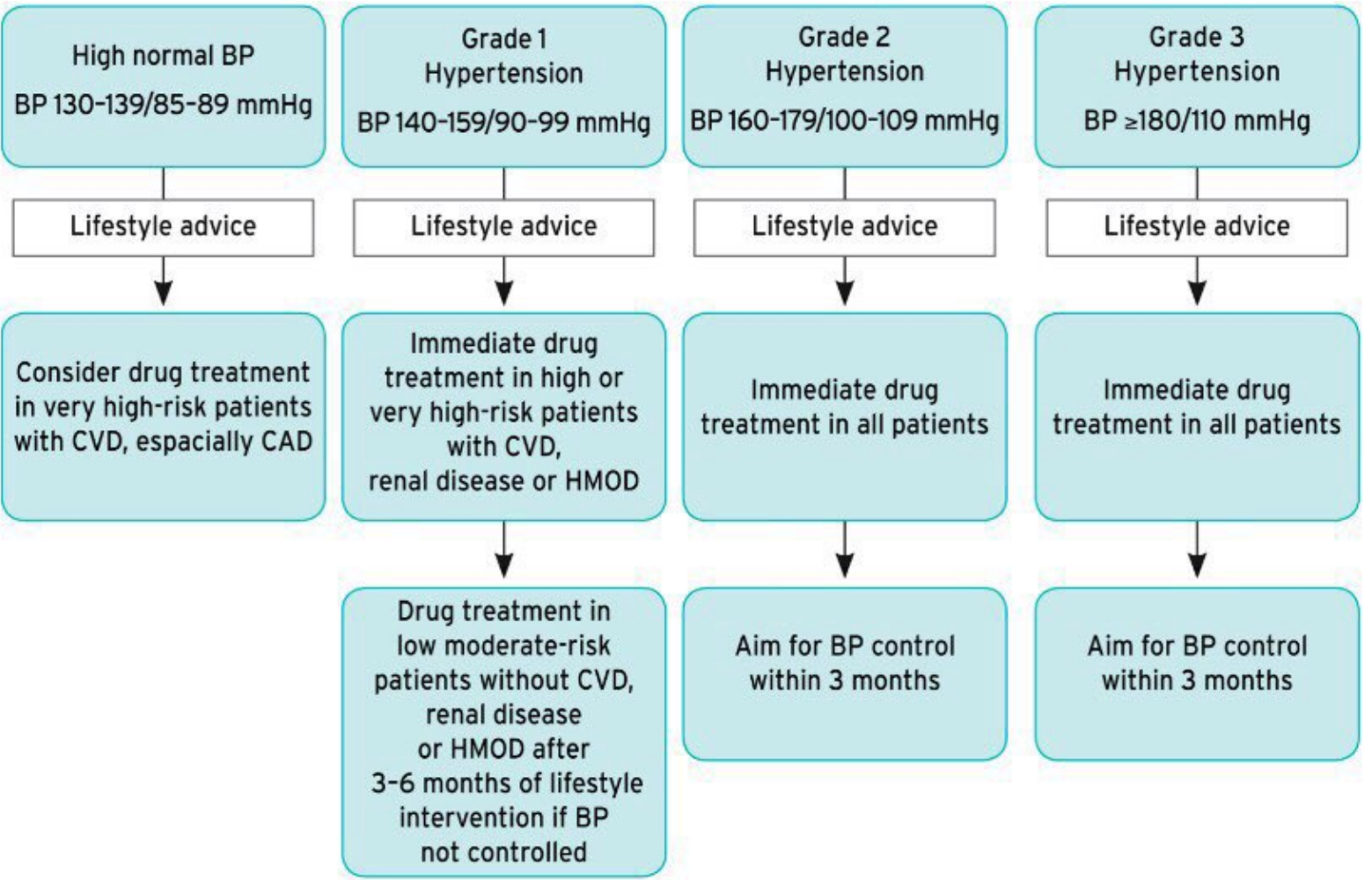
**Table 17 Summary of office blood pressure thresholds for treatment**

Age group	Office SBP treatment threshold (mmHg)					Office DBP treatment threshold (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18-65 years	≥140	≥140	≥140	≥140 <sup>a</sup>	≥140 <sup>a</sup>	≥90
65-79 years	≥140	≥140	≥140	≥140 <sup>a</sup>	≥140 <sup>a</sup>	≥90
≥80 years	≥160	≥160	≥160	≥160	≥160	≥90
Office DBP treatment threshold (mmHg)	≥90	≥90	≥90	≥90	≥90	

BP = blood pressure; CAD = coronary artery disease; CKD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

<sup>a</sup>Treatment may be considered in these very high-risk patients with high-normal [SBP](#) (i.e. [SBP](#) 130–140 mmHg).

**Figure 3 Initiation of BP-lowering treatment (lifestyle changes and medication) at different initial office [BP](#) levels**



BP = blood pressure; CAD = coronary artery disease; CVD = cardiovascular disease; HMOD = hypertension-mediated organ damage.



# Initiation of hypertension treatment according to office blood pressure

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Prompt initiation of BP-lowering drug treatment is recommended in patients with grade 2 or 3 hypertension at any level of <a href="#">CV</a> risk, simultaneous with the initiation of lifestyle changes.	I	A
In patients with grade 1 hypertension: <ul style="list-style-type: none"> <li>• Lifestyle interventions are recommended to determine if this will normalize <a href="#">BP</a>.</li> <li>• In patients with grade 1 hypertension at low-moderate risk and without evidence of <a href="#">HMOD</a>, BP-lowering drug treatment is recommended if the patient remains hypertensive after a period of lifestyle intervention.<sup>c</sup></li> <li>• In patients with grade 1 hypertension and at high-risk or with evidence of <a href="#">HMOD</a>, prompt initiation of drug treatment is recommended simultaneously with lifestyle interventions.</li> </ul>	IIa	B
	I	A
	I	A
In fit older patients with hypertension (even if age >80 years), BP-lowering drug treatment and lifestyle intervention are recommended when <a href="#">SBP</a> is ≥160 mmHg.	I	A
BP-lowering drug treatment and lifestyle intervention are recommended for fit older patients (>65 years but not >80 years) when <a href="#">SBP</a> is in the grade 1 range (140–159 mmHg), provided that treatment is well tolerated.	I	A



Antihypertensive treatment may also be considered in frail older patients if tolerated.	IIb	B
Withdrawal of BP-lowering drug treatment on the basis of age, even when patients attain an age of $\geq 80$ years, is not recommended, provided that treatment is well tolerated.	III	A
In patients with high-normal <a href="#">BP</a> (130–139/85–89 mmHg): <ul style="list-style-type: none"> <li>• Lifestyle changes are recommended</li> <li>• Drug treatment may be considered when their <a href="#">CV</a> is very high due to established <a href="#">CVD</a>, especially CAD.</li> </ul>	I	A
	IIb	A

BP = blood pressure; CAD = coronary artery disease; CV = cardiovascular; CVD = cardiovascular disease; HMOD = hypertension-mediated organ damage; SBP = systolic blood pressure.

<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence - <sup>c</sup>In patients with grade 1 hypertension and at low-to-moderate risk, drug treatment may be preceded by a prolonged period of lifestyle intervention to determine if this approach will normalize [BP](#). The duration of the lifestyle intervention alone will depend on the level of [BP](#) within the grade 1 range, i.e. the likelihood of achieving [BP](#) control with lifestyle intervention alone, and the opportunities for significant lifestyle change in individual patients.



# < BP treatment targets

The level to which [BP](#) should be lowered with drug treatment will depend on the patients' age, comorbidities and tolerability of treatment. A target range is recommended to indicate a lower safety boundary beyond which [BP](#) should not usually be lowered. Office [BP](#) target ranges are summarised below and in Table 18. Corresponding [BP](#) targets for home or ambulatory [BP](#) are less well validated but an office systolic [BP](#) <130mmHg probably corresponds to a 24hr [ABPM](#) systolic [BP](#) of <125mmHg and a home average systolic [BP](#) of <130mmHg.

Office blood pressure treatment targets in hypertensive patients		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
It is recommended that the first objective of treatment should be to lower <a href="#">BP</a> to <140/90 mmHg in all patients, and provided that the treatment is well tolerated, treated <a href="#">BP</a> values should be targeted to 130/80 mmHg or lower, in most patients.	I	A
In patients <65 years receiving BP-lowering drugs, it is recommended that <a href="#">SBP</a> should be lowered to a <a href="#">BP</a> range of 120–129 mmHg in most patients. <sup>c</sup>	I	A
In older patients (aged ≥65 years) receiving BP-lowering drugs: <ul style="list-style-type: none"><li>It is recommended that <a href="#">SBP</a> should be targeted to a <a href="#">BP</a> range of 130–139 mmHg.</li></ul>	I	A
<ul style="list-style-type: none"><li>Close monitoring of adverse effects is recommended.</li></ul>	I	C
<ul style="list-style-type: none"><li>These <a href="#">BP</a> targets are recommended for patients at any level of <a href="#">CV</a> risk and in patients with and without established <a href="#">CVD</a>.</li></ul>	I	A
A <a href="#">DBP</a> target of <80 mmHg should be considered for all hypertensive patients, independent of the level of risk and comorbidities.	IIa	B

BP = blood pressure; CV = cardiovascular; DBP = diastolic blood pressure; SBP = systolic blood pressure.  
<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence  
<sup>c</sup>Less evidence is available for this target in low–moderate-risk patients.

Table 18 Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke <sup>a</sup> /TIA	
18-65 years	Target to 130 or lower if tolerated Not <120	Target to 130 or lower if tolerated Not <120	Target to <140 to 130 if tolerated	Target to 130 or lower if tolerated Not <120	Target to 130 or lower if tolerated Not <120	70-79
65-79 years <sup>b</sup>	Target to 130-139 if tolerated	Target to 130-139 if tolerated	Target to 130-139 if tolerated	Target to 130-139 if tolerated	Target to 130-139 if tolerated	70-79
≥80 years <sup>b</sup>	Target to 130-139 if tolerated	Target to 130-139 if tolerated	Target to 130-139 if tolerated	Target to 130-139 if tolerated	Target to 130-139 if tolerated	70-79
Office DBP treatment threshold (mmHg)	70-79	70-79	70-79	70-79	70-79	

BP = blood pressure; CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.  
<sup>a</sup>Refers to patients with previous stroke and does not refer to [BP](#) targets immediately after acute stroke.  
<sup>b</sup>Treatment decisions and [BP](#) targets may need to be modified in older patients who are frail and independent.



Healthy lifestyle choices can prevent or delay the onset of hypertension and can reduce [CV](#) risk. Effective lifestyle changes may be sufficient to delay or prevent the need for drug therapy in patients with grade 1 hypertension and can also augment the effects of BP-lowering therapy in treated patients. However, lifestyle intervention should never delay the initiation of drug therapy in patients with [HMOD](#) or at a high level of [CV](#) risk. Recommended lifestyle measures that have been shown to reduce [BP](#) are shown below.

Adoption of lifestyle changes in patients with hypertension		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Salt restriction to <5 g per day is recommended.	I	A
It is recommended to restrict alcohol consumption to: <ul style="list-style-type: none"> <li>• Less than 14 units per week for men.</li> <li>• Less than 8 units per week for women.</li> </ul>	I	A
Increased consumption of vegetables, fresh fruits, fish, nuts, unsaturated fatty acids (olive oil), low consumption of red meat, and consumption of low-fat dairy products are recommended.	I	A
Body-weight control is indicated to avoid obesity ( <a href="#">BMI</a> >30 kg/m <sup>2</sup> or waist circumference >102 cm in men and >88 cm in women) and aim at a healthy <a href="#">BMI</a> (about 20–25 kg/m <sup>2</sup> ) and waist circumference values (<94 cm in men and <80 cm in women) to reduce <a href="#">BP</a> and <a href="#">CV</a> risk.	I	A
Regular aerobic exercise (e.g. at least 30 min of moderate dynamic exercise on 5–7 days per week) is recommended.	I	A
Smoking cessation and supportive care and referral to smoking cessation programs are recommended.	I	B
It is recommended to avoid binge drinking.	III	C

BMI = body mass index; BP = blood pressure; CV = cardiovascular.  
<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence mostly based on the effect on [BP](#) and/or [CV](#) risk profile.



Most hypertensive patients will require drug therapy in addition to lifestyle measures to achieve optimal [BP](#) control. Five major drug classes are recommended for the routine treatment of hypertension: ACE-inhibitors, ARBs, beta-blockers, CCBs, and diuretics (thiazides and thiazide-like diuretics such as chlorthalidone and indapamide), based on: (i) proven ability to reduce BP; (ii) evidence from placebo-controlled studies that they reduce [CV](#) events; and (iii) evidence of broad equivalence at reducing [CV](#) morbidity and mortality. Each of these drug classes has compelling or possible contraindications to their use (Table 19).

**Table 19 Compelling and possible contraindications to the use of specific antihypertensive drugs**

Drugs	Contraindications	
	Compelling	Possible
Diuretics (thiazides/thiazide-like, e.g. chlorthalidone and indapamide)	Gout	<ul style="list-style-type: none"> <li>• Metabolic syndrome</li> <li>• Glucose intolerance</li> <li>• Pregnancy</li> <li>• Hypercalcemia</li> <li>• Hypokalemia</li> </ul>
Beta-blockers	<ul style="list-style-type: none"> <li>• Asthma</li> <li>• Any high-grade sino-atrial or atrioventricular block</li> <li>• Bradycardia (heart rate &lt;60 beats per min)</li> </ul>	<ul style="list-style-type: none"> <li>• Metabolic syndrome</li> <li>• Glucose intolerance</li> <li>• Athletes and physically active patients</li> </ul>
Calcium antagonists (dihydropyridines)		<ul style="list-style-type: none"> <li>• Tachyarrhythmia</li> <li>• Heart failure (HFrEF, Class III or IV)</li> <li>• Pre-existing severe leg oedema</li> </ul>
Calcium antagonists (verapamil, diltiazem)	<ul style="list-style-type: none"> <li>• Any high-grade sino-atrial or atrioventricular block</li> <li>• Severe <a href="#">LV</a> dysfunction (<a href="#">LV</a> ejection fraction &lt;40%)</li> <li>• Bradycardia (heart rate &lt;60 beats per min)</li> </ul>	<ul style="list-style-type: none"> <li>• Constipation</li> </ul>
ACE-inhibitors	<ul style="list-style-type: none"> <li>• Pregnancy</li> <li>• Previous angioneurotic oedema</li> <li>• Hyperkalaemia (potassium &gt;5.5 mmol/L)</li> <li>• Bilateral renal artery stenosis</li> </ul>	<ul style="list-style-type: none"> <li>• Women of child-bearing potential without reliable contraception</li> </ul>
ARBs	<ul style="list-style-type: none"> <li>• Pregnancy</li> <li>• Hyperkalaemia (potassium &gt;5.5 mmol/L)</li> <li>• Bilateral renal artery stenosis</li> </ul>	<ul style="list-style-type: none"> <li>• Women of child-bearing potential without reliable contraception</li> </ul>

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; HFrEF = heart failure with reduced ejection fraction; LV = left ventricular.



## Overview

Despite the availability of proven and effective drug therapies for hypertension, the global rates of BP control remain poor. Thus, there is an urgent need to address the factors contributing to the poor control of BP in treated hypertensive patients, especially treatment inertia (clinician failure to up-titrate treatment) and poor patient adherence to multiple medications. The drug treatment algorithm has been developed to provide a simple and pragmatic treatment recommendation for the treatment of hypertension, based on a few key principles and recommendations:

1. The initiation of treatment in most patients should be with a single pill combination (SPC) of two drugs, to improve the speed, efficiency, and predictability of BP control. This normalises the concept that effective initial treatment of hypertension requires at least 2 drugs for most patients.
2. The preferred two-drug combinations are a RAS blocker (ACE-inhibitor or ARB) with a CCB or a diuretic. A beta-blocker in combination with a diuretic or any drug from the other major classes is an alternative, when there is a specific indication for a beta-blocker, e.g. angina, post-myocardial infarction, heart failure, or heart rate control.
3. Monotherapy should usually only be used as initial therapy for; (i) low-risk patients with stage 1 hypertension whose SBP is <150 mmHg, (ii) when it is decided to treat very high-risk patients with high-normal BP, or (iii) frail older patients.
4. A three-drug SPC comprising an RAS blocker + CCB + diuretic, should be used if BP is not controlled by a two-drug SPC.
5. Spironolactone is the preferred initial treatment for resistant hypertension, unless contraindicated (see section [here](#)).
6. Other classes of antihypertensive drugs may be used in the rare circumstances in which BP is not controlled by the above treatment strategy.

The core drug treatment algorithm is shown in [Figure 4](#), and variations in the algorithm for patients



Drug treatment strategy for hypertension		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Among all antihypertensive drugs, ACE-inhibitors, ARBs, beta-blockers, CCBs, and diuretics (thiazides and thiazide-like such as chlortalidone and indapamide) have demonstrated effective reduction of <a href="#">BP</a> and <a href="#">CV</a> events in RCTs, and thus are indicated as the basis of antihypertensive treatment strategies.	I	A
Combination treatment is recommended for most hypertensive patients as initial therapy. Preferred combinations should comprise a <a href="#">RAS</a> blocker (either an <a href="#">ACE</a> inhibitor or an ARB) with a <a href="#">CCB</a> or diuretic. Other combinations of the five major classes can be used	I	A
It is recommended that beta-blockers are combined with any of the other major drug classes when there are specific clinical situations, e.g. angina, post-myocardial infarction, heart failure, or heart rate control.	I	A
It is recommended to initiate an antihypertensive treatment with a two-drug combination, preferably in a <a href="#">SPC</a> . Exceptions are frail older patients and those at low risk and with grade 1 hypertension (particularly if <a href="#">SBP</a> is <150 mmHg).	I	B
It is recommended that if <a href="#">BP</a> is not controlledc with a two-drug combination, treatment should be increased to a three-drug combination, usually an <a href="#">RAS</a> blocker + <a href="#">CCB</a> + thiazide/thiazide-like diuretic, preferably as an <a href="#">SPC</a> .	I	A



# < Drug treatment strategy for HTN

as an [SPC](#).

It is recommended that if [BP](#) is not controlled<sup>c</sup> with a three-drug combination, treatment should be increased by the addition of spironolactone or, if not tolerated, other diuretics such as amiloride or higher doses of other diuretics, a beta-blocker, or an alpha-blocker.

The combination of two [RAS](#) blockers is not recommended.

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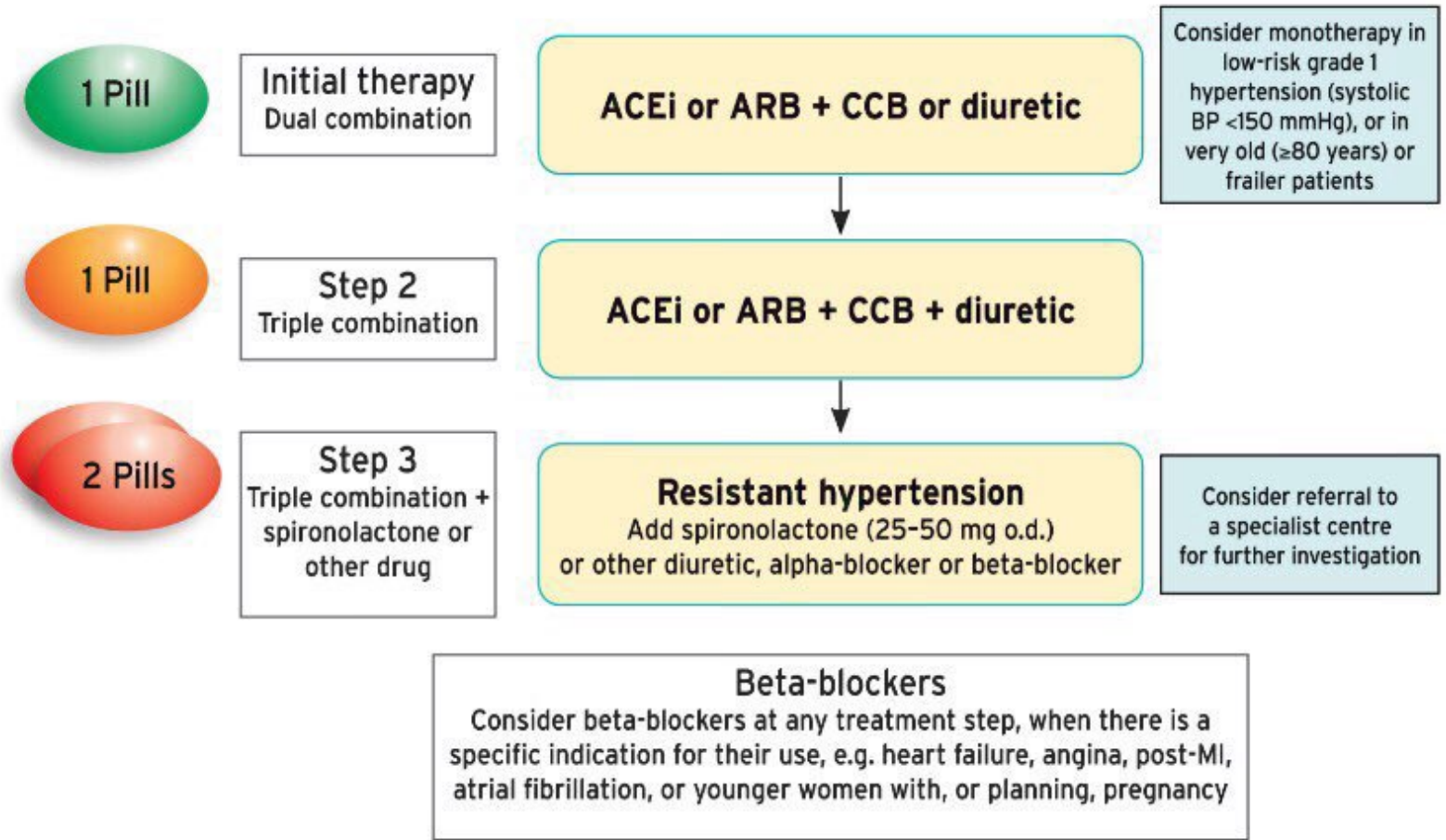
B

III

A

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium-channel blocker; CV = cardiovascular; RAS = renin–angiotensin system; RCT = randomized controlled trial; SBP = systolic blood pressure; SPC = single-pill combination.  
<sup>a</sup>Class of recommendation.  
<sup>b</sup>Level of evidence.  
<sup>c</sup>Adherence should be checked.

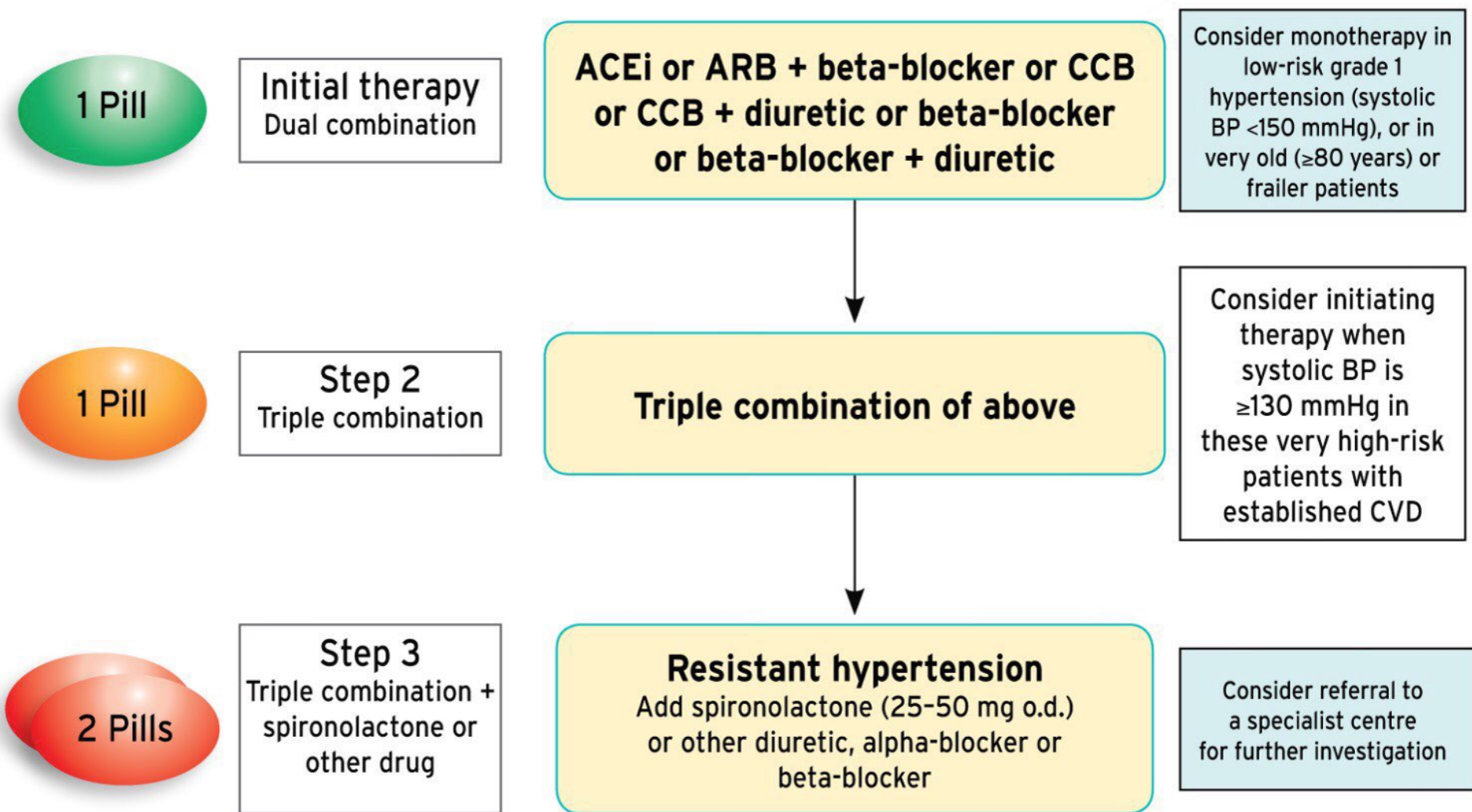
**Figure 4 Core drug-treatment strategy for uncomplicated hypertension. The core algorithm is also appropriate for most patients with hypertension-mediated organ damage (HMOD), cerebrovascular disease, diabetes, or peripheral artery disease (PAD)**



ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium-channel blocker; HMOD = hypertension-mediated organ damage; o.d. = omni die (every day); PAD = peripheral artery disease.



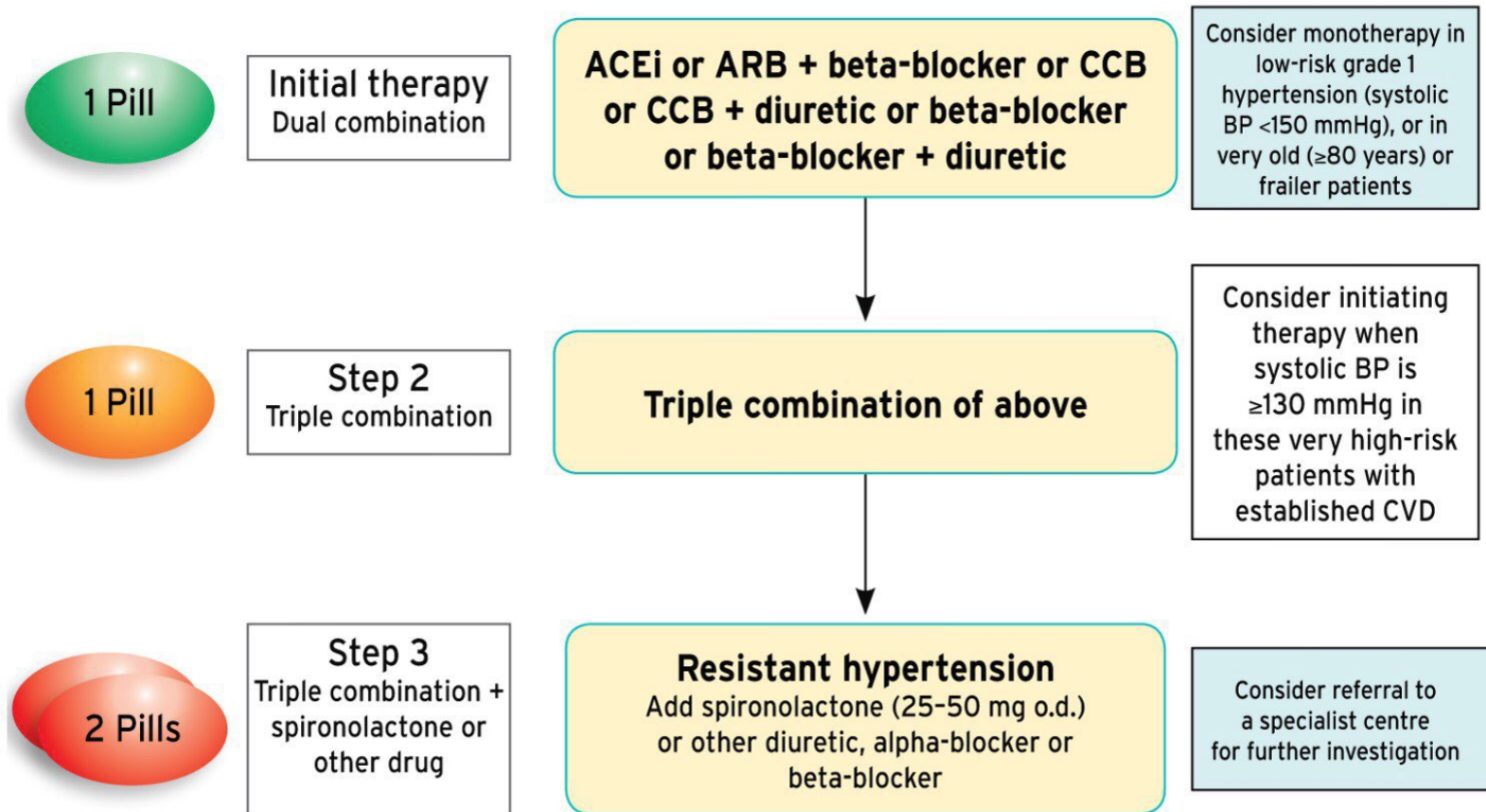
**Figure 5 Drug-treatment strategy for hypertension and coronary artery disease (CAD)**



ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CAD = coronary artery disease; CCB = calcium-channel blocker; CVD = cardiovascular disease; o.d. = omni die (every day).



**Figure 6 Drug-treatment strategy for hypertension and chronic kidney diseasea (CKD)**



ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium-channel blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; MI = myocardial infarction; o.d. = omni die (every day).

<sup>a</sup>CKD is defined as an [eGFR](#) <60 mL/min/1.72 m<sup>2</sup> with or without proteinuria.

<sup>b</sup>Use loop diuretics when [eGFR](#) is <30 mL/min/1.72 m<sup>2</sup> because thiazide/thiazide-like diuretics are much less effective/ineffective when [eGFR](#) is reduced to this level.

<sup>c</sup>Caution: risk of hyperkalaemia with spironolactone, especially when [eGFR](#) is <45 mL/min/1.72 m<sup>2</sup> or baseline K<sup>+</sup> ≥4.5 mmol/L.



**Figure 7 Drug-treatment strategy for hypertension and heart failure with reduced ejection fraction (HFrEF). Do not use non-dihydropyridine CCBs (e.g. verapamil or diltiazem).**

Initial therapy

**ACEi or ARB<sup>a</sup> + diuretic<sup>b</sup> (or loop diuretic)  
+ beta-blocker**



Step 2

**ACEi or ARB<sup>a</sup> + diuretic<sup>b</sup> (or loop diuretic)  
+ beta-blocker + MRA<sup>c</sup>**

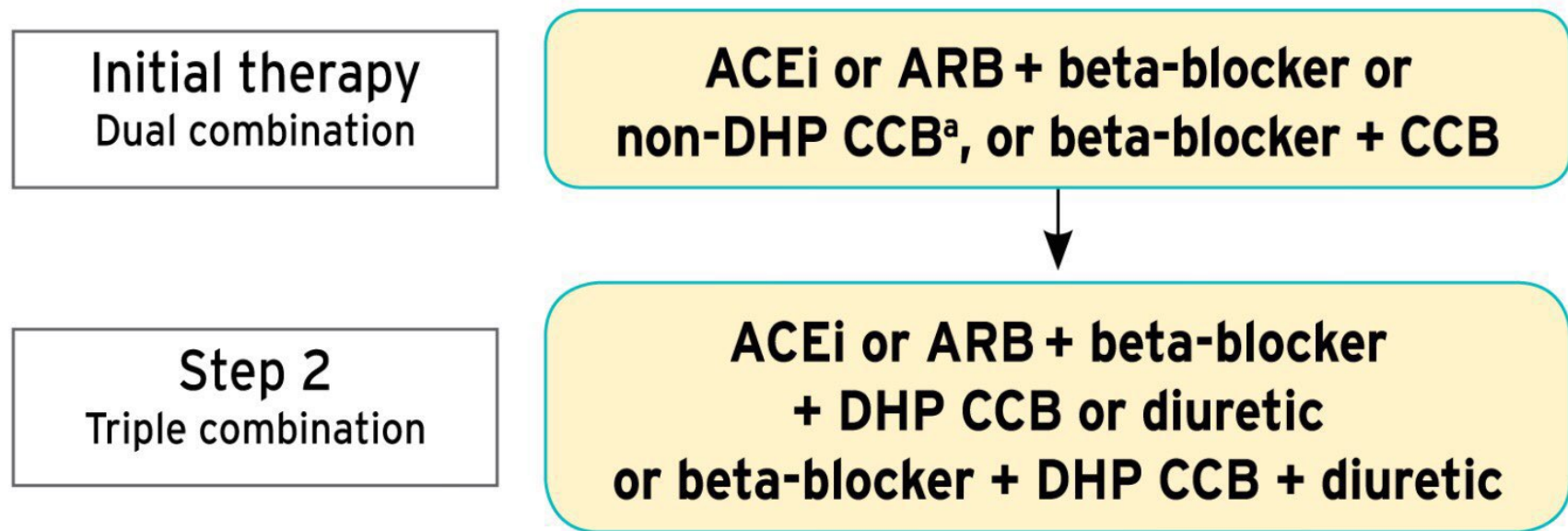
When antihypertensive therapy is not required in HFrEF, treatment should be prescribed according to the ESC Heart Failure Guidelines.<sup>136</sup>

ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist.

<sup>a</sup>Consider an angiotensin receptor/neprilysin inhibitor instead of ACEi or [ARB](#) per [ESC](#) Heart Failure Guidelines. <sup>b</sup>Diuretic refers to thiazide/thiazide-like diuretic. Consider a loop diuretic as an alternative in patients with oedema. <sup>c</sup>MRA (spironolactone or eplerenone).



**Figure 8 Drug-treatment strategy for hypertension and atrial fibrillation (AF)**



Add oral anticoagulation when indicated according to the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, unless contraindicated.

<sup>a</sup>Routine combination of beta-blockers with non-dihydropyridine CCBs (e.g. verapamil or diltiazem) is not recommended due to a potential marked reduction in heart rate.

ACEi = angiotensin-converting enzyme inhibitor; AF = atrial fibrillation; ARB = angiotensin receptor blocker; CCB = calcium-channel blocker; CHA<sub>2</sub>DS<sub>2</sub>-VASc = Cardiac failure, Hypertension, Age ≥75 [Doubled], Diabetes, Stroke [Doubled] – Vascular disease, Age 65–74 and Sex category [Female]; DHP = dihydropyridine.

<sup>a</sup>Non-dihydropyridine [CCB](#) (non-DHP [CCB](#), e.g. verapamil or diltiazem).



Device-based therapy for hypertension is a fast-moving field. Although some positive data has emerged from recent small sham-controlled studies, especially with renal denervation, further sham-controlled studies are needed before devicebased therapies can be recommended for the routine treatment of hypertension outside of the framework of clinical trials.

Device-based therapies for hypertension		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Use of device-based therapies is not recommended for the routine treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	III	B

<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.



## Definition of resistant hypertension

Hypertension is defined as resistant to treatment when the recommended treatment strategy (see above) fails to lower office **BP** to below 140/90 mmHg, and inadequate **BP** control is confirmed by **ABPM** or **HBPM**, in patients whose adherence to therapy has been confirmed.

The recommended treatment strategy should include appropriate lifestyle measures and treatment with optimal or best-tolerated doses of three or more drugs that should include a diuretic and typically an ACE-inhibitor or **ARB**, and a **CCB**. Pseudoresistant hypertension (see below) and secondary causes of hypertension should also have been excluded (see section 6). Patient characteristics, causes and factors contributing to resistant hypertension are shown in Table 20.

Table 20 Resistant hypertension: Patient characteristics, secondary causes, and contributing factors		
Characteristics of patients with resistant hypertension	Causes of secondary resistant hypertension	Drugs and substances that may cause raised <b>BP</b>
<b>Demographics</b> <ul style="list-style-type: none"> <li>• Older age (especially &gt;75 years)</li> <li>• Obesity</li> <li>• More common in black people</li> <li>• Excess dietary sodium intake</li> <li>• High baseline <b>BP</b> and chronicity of uncontrolled hypertension</li> </ul>	<b>More common causes</b> <ul style="list-style-type: none"> <li>• Primary hyperaldosteronism</li> <li>• Atherosclerotic renovascular disease</li> <li>• Sleep apnoea</li> <li>• CKD</li> </ul>	<b>Prescribed drugs</b> <ul style="list-style-type: none"> <li>• Oral contraceptives</li> <li>• Sympathomimetic agents (e.g. decongestants in proprietary cold remedies)</li> <li>• Non-steroidal antiinflammatory drugs</li> <li>• Cyclosporin</li> <li>• Erythropoietin</li> <li>• Steroids (e.g. prednisolone, hydrocortisone)</li> <li>• Some cancer therapies</li> </ul>
<b>Concomitant disease</b> <ul style="list-style-type: none"> <li>• HMOD: <b>LVH</b> and/or <b>CKD</b></li> <li>• Diabetes</li> <li>• Atherosclerotic vascular disease</li> <li>• Aortic stiffening and isolated systolic hypertension</li> </ul>	<b>Uncommon causes</b> <ul style="list-style-type: none"> <li>• Pheochromocytoma</li> <li>• Fibromuscular dysplasia</li> <li>• Aortic coarctation</li> <li>• Cushing's disease</li> <li>• Hyperparathyroidism</li> </ul>	<b>Non-prescription drugs</b> <ul style="list-style-type: none"> <li>• Recreational drugs (e.g. cocaine, amphetamines, anabolic steroids)</li> <li>• Excess liquorice ingestion</li> <li>• Herbal remedies (e.g. ephedra, ma huang)</li> </ul>

BP = blood pressure; CKD = chronic kidney disease; HMOD = hypertension-mediated organ damage; LVH = left ventricular hypertrophy.





- 1. Poor adherence to prescribed medicines**
- 2. White-coat phenomenon:** Office BP is elevated but BP is controlled with ABPM or HBPM.
- 3. Poor office-BP measurement technique:** Cuffs that are too small relative to the arm circumference, can result in a spurious elevation of BP
- 4. Marked brachial artery calcification:** Usually in older patients with heavily calcified arteries.
- 5. Clinician inertia:** Resulting in inadequate doses or irrational combinations of BP-lowering drugs



Effective treatment combines lifestyle changes (especially reducing sodium intake), discontinuation of interfering substances, and the sequential addition of antihypertensive drugs to the initial triple therapy (usually an ACE-inhibitor or [ARB](#) + [CCB](#) + diuretic). Low dose spironolactone (25-50mg per day) is an effective treatment for resistant hypertension, however, its efficacy and safety has not been established in patients with significant renal impairment. Consequently, the use of spironolactone for resistant hypertension should usually be restricted to patients with an [eGFR](#) ≥45 mL/min and a plasma potassium concentration of ≤4.5 mmol/L. Electrolytes and [eGFR](#) should be monitored soon after initiation. Amiloride (10–20 mg/day) has recently been shown to be as effective as spironolactone (25–50 mg daily) but has the same limitations with regard to renal function and potassium. A loop diuretic should replace thiazides/thiazide-like diuretics if the [eGFR](#) is <30 mL/min.

Resistant hypertension		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<p>It is recommended that hypertension be defined as resistant to treatment (i.e. resistant hypertension) when:</p> <ul style="list-style-type: none"><li>• Optimal doses (or best-tolerated doses) of an appropriate therapeutic strategy, which should include a diuretic (typically an ACE-inhibitor or <a href="#">ARB</a> + <a href="#">CCB</a> + thiazide/thiazide-like diuretic), fails to lower clinic <a href="#">SBP</a> and <a href="#">DBP</a> values to &lt;140 mmHg and/or &lt;90 mmHg, respectively; and</li><li>• The inadequate control of <a href="#">BP</a> has been confirmed by <a href="#">ABPM</a> or HBPM; and</li><li>• After exclusion of various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension.</li></ul>	I	C
Recommended treatment of re		



hypertension (especially poor medication adherence) and secondary hypertension.		
Recommended treatment of resistant hypertension is: <ul style="list-style-type: none"><li>• Reinforcement of lifestyle measures, especially sodium restriction.</li><li>• Addition of low-dose spironolactone<sup>c</sup> to existing treatment.</li><li>• Or the addition of further diuretic therapy if intolerant to spironolactone, with either eplerenone,<sup>c</sup> amiloride,<sup>c</sup> higher dose thiazide/thiazide-like diuretic, or a loop diuretic.<sup>d</sup></li><li>• Or the addition of bisoprolol or doxazosin.</li></ul>	I	B

ABPM = ambulatory blood pressure monitoring; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium-channel blocker; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; HBPM = home blood pressure monitoring.

<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.

<sup>c</sup>When spironolactone is not tolerated, replace with amiloride or eplerenone. The use of these drugs should be restricted to patients with an estimated glomerular filtration rate  $\geq 45$  mL/min and a plasma potassium concentration of  $\leq 4.5$  mmol/L, because of the risk of hyperkalaemia.

<sup>d</sup>A loop diuretic should replace thiazides/thiazide-like diuretics if the estimated glomerular filtration rate is  $< 30$  mL/min.



Secondary hypertension is hypertension due to an identifiable cause, which may be treatable with an intervention specific to the cause. A high index of suspicion (see [Table 21](#)) and early detection of secondary causes of hypertension is important because interventions may be curative, especially in younger patients. Common causes of secondary hypertension and screening investigations are shown in [Tables 22](#) and [23](#). Some medications may also increase [BP](#) and these are listed in [Table 24](#).



**Table 21 Patient characteristics that should raise the suspicion of secondary hypertension**

Characteristic
Younger patients (<40 years) with grade 2 hypertension or onset of any grade of hypertension in childhood
Acute worsening hypertension in patients with previously documented chronically stable normotension
Resistant hypertension
Severe (grade 3) hypertension or a hypertension emergency
Presence of extensive hypertension-mediated organ damage
Clinical or biochemical features suggestive of endocrine causes of hypertension or <a href="#">CKD</a>
Clinical features suggestive of obstructive sleep apnoea
Symptoms suggestive of pheochromocytoma or family history of pheochromocytoma

CKD = chronic kidney disease; HMOD = hypertension-mediated organ damage.



# < Secondary HTN - characteristics

Table 22 Common causes of secondary hypertension

Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Obstructive sleep apnoea	5-10%	Snoring; obesity (can be present in non-obese); morning headache; daytime somnolence	Epworth score + ambulatory polygraphy
Renal parenchymal disease	2-10%	Mostly asymptomatic; diabetes; haematuria, proteinuria, nocturia; anaemia, renal mass in adult polycystic CKD	Plasma creatinine and electrolytes, eGFR; urine dipstick for blood and protein, urinary albumin:creatinine ratio; renal ultrasound
Renovascular disease			
Atherosclerotic renovascular disease	1-10%	Older; widespread atherosclerosis (especially PAD); diabetes; smoking; recurrent flash pulmonary oedema; abdominal bruit	Duplex renal artery Doppler or CT angiography or MR angiography
Fibromuscular dysplasia		Younger; more common in women; abdominal bruit	
Primary Aldosteronism	5-15%	Mostly asymptomatic; muscle weakness (rare)	Plasma aldosterone and renin, and aldosterone: renin ratio; hypokalaemia (in a minority): note hypokalaemia can depress aldosterone levels
Phaeochromocytoma	<1%	Episodic symptoms (the 5 'Ps'): paroxysmal hypertension, pounding headache, perspiration, palpitations, and pallor; labile BP; BP surges precipitated by drugs (e.g. betablockers, metoclopramide, sympathomimetics, opioids, and tricyclic antidepressants)	Plasma or 24 h urinary fractionated metanephrines
Cushing's syndrome	<1%	Moon face, central obesity, skin atrophy, striae and bruising; diabetes; chronic steroid use	24-h urinary free cortisol
Thyroid disease (hyper- or hypothyroidism)	1-2%	Signs and symptom of hyper- or hypothyroidism	Thyroid function tests
Hyperparathyroidism	<1%	Hypercalcaemia, hypophosphatemia	Parathyroid hormone, Ca <sup>2+</sup>
Coarctation of the aorta			
Coarctation of the aorta	<1%	Usually detected in children or adolescence; different BP (≥20/10 mmHg) between upper-lower extremities and/or between right-left arm and delayed radial-femoral femoral pulsation; low ABI interscapular ejection murmur; rib notching on chest X-ray	Echocardiogram

ABI = ankle–brachial index; BP = blood pressure; CKD = chronic kidney disease; CT = computed tomography; eGFR = estimated glomerular filtration rate; PAD = peripheral artery disease.



**Table 23 Incidence and typical causes of secondary hypertension according to age**

Age group	Per cent with underlying cause	Typical causes
Young children (<12 years)	70–85	Renal parenchymal disease Coarctation of the aorta Monogenic disorders
Adolescents (12–18 years)	10–15	Renal parenchymal disease Coarctation of the aorta Monogenic disorders
Young adults (19–40 years)	5–10	Renal parenchymal disease Fibromuscular dysplasia (especially in women) Undiagnosed monogenic disorders
Middle-aged adults (41–65 years)	5–15	Primary aldosteronism Obstructive sleep apnoea Cushing’s syndrome Pheochromocytoma Renal parenchymal disease Atherosclerotic renovascular disease
Older adults (<65 years)	5–10	Atherosclerotic renovascular disease Renal parenchymal disease Thyroid disease



**Table 24 Medications and other substances that may increase blood pressure**

**Medication/substance**

Oral contraceptive pill	Especially oestrogen containing – cause hypertension in ~5% of women, usually mild but can be severe
Diet pills	For example, phenylpropanolamine and sibutramine
Nasal decongestants	For example, phenylephrine hydrochloride and naphazoline hydrochloride
Stimulant drugs	Amphetamine, cocaine, and ecstasy – these substances usually cause acute rather than chronic hypertension
Liquorice	Chronic excessive liquorice use mimics hyperaldosteronism by stimulating the mineralocorticoid receptor and inhibiting cortisol metabolism
Immunosuppressive medications	For example, cyclosporin A (tacrolimus has less effect on <a href="#">BP</a> and rapamycin has almost no effect on BP), and steroids (e.g. corticosteroids, hydrocortisone)
Antiangiogenic cancer therapies	Antiangiogenic drugs, such as <a href="#">VEGF</a> inhibitors (e.g. bevacizumab), tyrosine kinase inhibitors (e.g. sunitinib), and sorafenib, have been reported to increase <a href="#">BP</a>
Other drugs and substances that may raise <a href="#">BP</a>	Anabolic steroids, erythropoietin, non-steroidal antiinflammatory drugs, herbal remedies (e.g. ephedra, ma huang)

BP = blood pressure; VEGF = vascular endothelial growth factor.



Hypertension emergencies are situations in which severe hypertension (usually grade 3) is associated with acute organ damage, which is often life-threatening and requires immediate but careful intervention to lower [BP](#), in hospital, usually with intravenous (i.v.) therapy. Typical presentations of a hypertension emergency are:

- [Patients with malignant hypertension](#), characterised by severe hypertension (usually grade 3) associated with characteristic funduscopic changes (flame haemorrhages and/or papilloedema), microangiopathy, and disseminated intravascular coagulation, encephalopathy (in about 15% of cases), acute heart failure, and acute deterioration in renal function. The term “malignant” reflects the very poor prognosis for this condition if untreated.
- [Patients with severe hypertension associated with other clinical conditions](#) likely to require an urgent reduction of [BP](#), e.g. acute aortic dissection, acute myocardial ischaemia, or acute heart failure.
- [Patients with sudden severe hypertension due to pheochromocytoma](#)
- [Pregnant women with severe hypertension or pre-eclampsia](#)

The term “***hypertension urgency***” has also been used to describe severe hypertension presenting to the emergency department in patients in whom there is no clinical evidence of acute [HMOD](#). Whilst these patients require [BP](#) reduction, they rarely require admission to hospital, and [BP](#) reduction is best achieved with oral medication according to the drug treatment algorithm shown in [Figures 4-8](#). These patients will require urgent outpatient review to ensure their [BP](#) is coming under control.

### Table 25 Diagnostic work-up for patients with a suspected hypertension emergency

#### Common tests for all potential causes

Fundoscopy is a critical part of the diagnostic work-up

12-lead [ECG](#)

Haemoglobin, platelet count, fibrinogen

Creatinine, [eGFR](#), electrolytes, [LDH](#), haptoglobin

Urine albumin:creatinine ratio, urine microscopy for red cells, leucocytes, and casts

Pregnancy test in women of child-bearing age

#### Specific tests by indication

Troponin, [CK-MB](#) (in suspected cardiac involvement, e.g. acute chest pain or acute heart failure) and [NT-proBNP](#)

Chest X-ray (fluid overload)

Echocardiography (aortic dissection, heart failure, or ischaemia)

[CT](#) angiography of thorax and/or abdomen in suspected acute aortic disease (e.g. aortic dissection)

[CT](#) or [MRI](#) brain (nervous system involvement)

Renal ultrasound (renal impairment or suspected renal artery stenosis)

Urine drug screen (suspected methamphetamine or cocaine use)

CK-MD = creatine kinase-muscle/brain; CT = computed tomography; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; LDH = lactate dehydrogenase; MRI = magnetic resonance imaging; NT-proBNP = N-terminal pro-B natriuretic peptide.



- [CT](#) angiography of thorax and/or abdomen in suspected acute aortic disease (e.g. aortic dissection)
- [CT](#) or [MRI](#) brain (nervous system involvement)
- Renal ultrasound (renal impairment or suspected renal artery stenosis)
- Urine drug screen (suspected methamphetamine or cocaine use)

CK-MD = creatine kinase-muscle/brain; CT = computed tomography; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; LDH = lactate dehydrogenase; MRI = magnetic resonance imaging; NT-proBNP = N-terminal pro-B natriuretic peptide.

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Table 26 Hypertensive emergencies requiring immediate <a href="#">BP</a> lowering with i.v. drug therapy			
Clinical presentation	Timeline and target for <a href="#">BP</a> reduction	First-line treatment	Alternative
Malignant hypertension with or without acute renal failure	Several hours Reduce <a href="#">MAP</a> by 20–25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediately reduce <a href="#">MAP</a> by 20–25%	Labetalol Nicardipine	Nitroprusside
Acute coronary event	Immediate reduce <a href="#">SBP</a> to <140 mmHg	Nitroglycerine Labetalol	Urapidil
Acute cardiogenic pulmonary oedema	Immediately reduce <a href="#">SBP</a> to <140 mmHg	Nitroprusside OR nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic dissection	Immediately reduce <a href="#">SBP</a> to <120 mmHg AND heart rate to <60 bpm	Esmolol AND nitroprusside OR nitroglycerine OR nicardipine	Labetalol OR metoprolol
Eclampsia and severe pre-eclampsia/HELLP	Immediately reduce <a href="#">SBP</a> to <160 mmHg AND <a href="#">DBP</a> to <105 mmHg	Labetalol OR nicardipine AND magnesium sulphate	Consider delivery

BP = blood pressure; BPM = beats per minute; DBP = diastolic blood pressure; HELLP = haemolysis, elevated liver enzymes, low platelets; i.v. = intravenous; MAP = mean arterial pressure; SBP = systolic blood pressure.



Hypertensive disorders in pregnancy remain a major cause of maternal, foetal, and neonatal morbidity and mortality.

The definition of hypertension in pregnancy is based on office BP values, SBP  $\geq 140$  mmHg and/or DBP  $\geq 90$  mmHg. Hypertension in pregnancy is classified as mild (140–159/90–109 mmHg) or severe ( $\geq 160/110$  mmHg), in contrast to the conventional hypertension grading.

Hypertension in pregnancy is not a single entity but comprises:

- **Pre-existing hypertension:** precedes pregnancy or develops before 20 weeks of gestation and usually persists for more than 6 weeks post-partum and may be associated with proteinuria.
- **Gestational hypertension:** develops after 20 weeks of gestation and usually resolves within 6 weeks post-partum.
- **Pre-existing hypertension plus superimposed gestational hypertension with proteinuria.**
- **Pre-eclampsia:** gestational hypertension with significant proteinuria ( $>0.3$  g/24 h or  $\geq 30$  mg/mmol albumin: creatinine ratio). It is more frequent in the first pregnancy, in multiple pregnancy, in hydatidiform mole, in antiphospholipid syndrome, or with pre-existing hypertension, renal disease, or diabetes. The only cure for pre-eclampsia is delivery. Pre-eclampsia should be suspected when hypertension is accompanied by headache, visual disturbances, abdominal pain, or abnormal laboratory tests, specifically low platelets and/or abnormal liver function - proteinuria may be a late manifestation of pre-eclampsia.



Management of hypertension in pregnancy		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In women with gestational hypertension or pre-existing hypertension superimposed by gestational hypertension, or with hypertension and subclinical organ damage or symptoms, initiation of drug treatment is recommended when <a href="#">SBP</a> is ≥140 or <a href="#">DBP</a> ≥90 mmHg.	I	C
In all other cases, initiation of drug treatment is recommended when <a href="#">SBP</a> is ≥150 mmHg or <a href="#">DBP</a> is ≥95 mmHg.	I	C
Methyldopa, labetalol, and CCBs are recommended as the drugs of choice for the treatment of hypertension in pregnancy	I	B (Methyldopa)
	I	C (Labetalol or CCBs)
ACE-inhibitors, ARBs, or direct renin inhibitors are not recommended during pregnancy.	III	C
<a href="#">SBP</a> ≥170 mmHg or <a href="#">DBP</a> ≥110 mmHg in a pregnant woman is an emergency, and admission to hospital is recommended.	I	C
In severe hypertension, drug treatment with i.v. labetalol or oral methyldopa or nifedipine is recommended.	I	C
The recommended treatment for hypertensive crisis is i.v. labetalol or nicardipine and magnesium.	I	C
In pre-eclampsia associated with pulmonary oedema, nitroglycerin given as an i.v. infusion is recommended.	I	C
In women with gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks.	I	B
It is recommended to expedite delivery in pre-eclampsia with adverse conditions such as visual disturbances or haemostatic disorders.	I	C

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium-channel blocker; DBP = diastolic blood pressure; i.v. = intravenous; SBP = systolic blood pressure.  
<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.



Patients with white coat hypertension have an elevated office BP but their BP is normal on home BP monitoring and/or 24hr ABPM. It is most common in patients with grade 1 hypertension on office BP measurement and it is unlikely that home BP or ABPM will be normal in patients with grade 2 hypertension on office BP. White coat hypertension is not benign with the risk intermediate between normotension and sustained hypertension. Routine drug treatment is not indicated for white coat hypertension but lifestyle interventions are recommended. Long term periodic review of these patients is important because many will develop an elevated BP on home BP monitoring or ABPM, which will require drug treatment.



Patients with masked hypertension have an office which appears normal i.e. BP <140/90mmHg but their BP is elevated BP on home BP monitoring or 24hr ABPM. Masked hypertension is more common in patients with a high normal BP on office BP measurement and should be suspected when HMOD is present. These patients are at increased CV risk, equivalent to that in patients with sustained hypertension. These patients should be advised to implement lifestyle changes and drug treatment should be considered because of their increased CV risk, with the aim of normalising their out of office BP levels.



Management of white-coat hypertension		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In white-coat hypertensive patients, it is recommended to implement lifestyle changes aimed at reducing <a href="#">CV</a> risk as well as a regular follow-up with periodic out-of-office <a href="#">BP</a> monitoring.	I	C
In patients with white-coat hypertension:		
• Drug treatment may be considered in people with evidence of <a href="#">HMOD</a> or in whom <a href="#">CV</a> risk is high or very high.	IIb	C
• Routine drug treatment is not indicated.	III	C
BP = blood pressure; CV = cardiovascular; HMOD = hypertension-mediated organ damage. <sup>a</sup> Class of recommendation - <sup>b</sup> Level of evidence.		

Management of masked hypertension		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In masked hypertension, lifestyle changes are recommended to reduce <a href="#">CV</a> risk, with regular follow-up, including periodic out-of-office <a href="#">BP</a> monitoring.	I	C
Antihypertensive drug treatment should be considered in masked hypertension to normalize the out-of-office <a href="#">BP</a> based on the prognostic importance of out-of-office <a href="#">BP</a> elevation.	IIa	C
Antihypertensive drug uptitration should be considered in treated patients whose out-of-office <a href="#">BP</a> is not controlled (i.e. masked uncontrolled hypertension), because of the high <a href="#">CV</a> risk of these patients.	IIa	C
BP = blood pressure; CV = cardiovascular. <sup>a</sup> Class of recommendation - <sup>b</sup> Level of evidence.		



The management of hypertension can be influenced by the presence of comorbidities. The drug treatment algorithms for hypertension associated with various comorbidities are shown in figures 4-8 and the recommended therapeutic strategies for specific comorbidities are listed in next chapters.



Treatment strategies in people with diabetes		
Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Antihypertensive drug treatment is recommended for people with diabetes when office <a href="#">BP</a> is $\geq 140/90$ mmHg.	I	A
In people with diabetes receiving BP-lowering drugs it is recommended: <ul style="list-style-type: none"> <li>• To target <a href="#">SBP</a> to 130 mmHg and <math>&lt; 130</math> mmHg, if tolerated, but not <math>&lt; 120</math> mmHg.</li> <li>• In older people (aged <math>\geq 65</math> years), to target to a <a href="#">SBP</a> range of 130–139 mmHg.</li> <li>• To target the <a href="#">DBP</a> to <math>&lt; 80</math> mmHg, but not <math>&lt; 70</math> mmHg.</li> </ul>	I  I  I	A  A  C
It is recommended to initiate treatment with a combination of an <a href="#">RAS</a> blocker with a <a href="#">CCB</a> or thiazide/thiazide-like diuretic. <sup>c</sup>	I	A
Simultaneous administration of two <a href="#">RAS</a> blockers, e.g. and ACE-inhibitor and <a href="#">ARB</a> , is not indicated.	III	A

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium-channel blocker; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; RAS = renin–angiotensin system; SBP = systolic blood pressure. <sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence - <sup>c</sup>When [eGFR](#)  $< 30$  mL/min/1.73 m<sup>2</sup>, avoid thiazide/thiazide-like diuretics and consider using a loop diuretic when a diuretic is required.



# Therapeutic strategies for treatment of hypertension in Chronic Kidney Disease

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In patients with diabetic or non-diabetic <a href="#">CKD</a> , it is recommended that an office <a href="#">BP</a> of $\geq 140/90$ mmHg be treated with lifestyle advice and BP-lowering medication.	I	A
In patients with diabetic or non-diabetic CKD:	I	A
<ul style="list-style-type: none"> <li>It is recommended to lower <a href="#">SBP</a> to a range of 130–139 mmHg.</li> <li>Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes.</li> </ul>	IIa	C
<a href="#">RAS</a> blockers are more effective at reducing albuminuria than other antihypertensive agents, and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria.	I	A
A combination of a <a href="#">RAS</a> blocker with a <a href="#">CCB</a> or a diuretic <sup>c</sup> is recommended as initial therapy.	I	A
A combination of two <a href="#">RAS</a> blockers is not recommended.	III	A

BP = blood pressure; CCB = calcium-channel blocker; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; RAS = renin–angiotensin system; SBP = systolic blood pressure.  
<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence - <sup>c</sup>In case of [eGFR](#)  $< 30$  mL/min/1.73 m<sup>2</sup>, avoid thiazide/ thiazide-like diuretic and consider using a loop diuretic if



Therapeutic strategies in hypertensive patients with coronary artery disease

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In patients with CAD receiving BP-lowering drugs, it is recommended: <ul style="list-style-type: none"><li>• To target <a href="#">SBP</a> ≤130 mmHg and lower, if tolerated, but not &lt;120 mmHg.</li><li>• In older patients (aged ≥65 years), to target to a <a href="#">SBP</a> range of 130–140 mmHg.</li><li>• To target <a href="#">DBP</a> to &lt;80 mmHg, but not &lt;70 mmHg.</li></ul>	I	A
	I	A
	I	C
In hypertensive patients with a history of myocardial infarction, beta-blockers and <a href="#">RAS</a> blockers are recommended as part of treatment.	I	A
In patients with symptomatic angina, beta-blockers ad/or CCBs are recommended.	I	A

BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; DBP = diastolic blood pressure; RAS = renin–angiotensin system; SBP = systolic blood pressure  
<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.



# Therapeutic strategies in hypertensive patients with coronary artery disease

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<p>In patients with CAD receiving BP-lowering drugs, it is recommended:</p> <ul style="list-style-type: none"> <li>To target <a href="#">SBP</a> ≤130 mmHg and lower, if tolerated, but not &lt;120 mmHg.</li> <li>In older patients (aged ≥65 years), to target to a <a href="#">SBP</a> range of 130–140 mmHg.</li> <li>To target <a href="#">DBP</a> to &lt;80 mmHg, but not &lt;70 mmHg.</li> </ul>	I	A
	I	A
	I	C
In hypertensive patients with a history of myocardial infarction, beta-blockers and <a href="#">RAS</a> blockers are recommended as part of treatment.	I	A
In patients with symptomatic angina, beta-blockers ad/or CCBs are recommended.	I	A

BP = blood pressure; CAD = coronary artery disease; CCB = calcium channel blocker; DBP = diastolic blood pressure; RAS = renin–angiotensin system; SBP = systolic blood pressure  
<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.

# Therapeutic strategies in hypertensive patients with heart failure or Left Ventricular Hypertrophy

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In hypertensive patients with heart failure (with reduced or preserved ejection fraction), BP-lowering treatment should be considered if <a href="#">BP</a> is $\geq 140/90$ mmHg.	IIa	B
In patients with <a href="#">HFrEF</a> , it is recommended that BP-lowering treatment comprises an ACE-inhibitor or <a href="#">ARB</a> and a beta-blocker and diuretic and/or mineralocorticoid receptor antagonist if required.	I	A
Dihydropyridine CCBs may be added if <a href="#">BP</a> control is not achieved.	IIb	C
In patients with <a href="#">HFpEF</a> , BP-treatment threshold and target values should be the same as for <a href="#">HFrEF</a> .	IIa	B
Because no specific drug has proven its superiority, all major agents can be used.	I	C
In all patients with LVH:	I	A
<ul style="list-style-type: none"> <li>It is recommended to treat with an <a href="#">RAS</a> blocker in combination with a <a href="#">CCB</a> or diuretic.</li> <li><a href="#">SBP</a> should be lowered to a range of 120–130 mmHg.</li> </ul>	IIa	B

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; CCB = calcium-channel blocker; HFrEF = heart failure with reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; LVH = left ventricular hypertrophy; RAS = renin–angiotensin system; SBP = systolic blood pressure. <sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.



# Therapeutic strategies in hypertensive patients with acute stroke and cerebrovascular disease

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<p>In patients with acute intracerebral haemorrhage:</p> <ul style="list-style-type: none"> <li>• Immediate <a href="#">BP</a> lowering is not recommended for patients with <a href="#">SBP</a> &lt;220 mmHg.</li> <li>• In patients with <a href="#">SBP</a> ≥220 mmHg, careful acute <a href="#">BP</a> lowering with i.v. therapy, to &lt;180 mmHg should be considered.</li> </ul>	III	A
	IIa	B
<p>In acute ischaemic stroke, routine <a href="#">BP</a> lowering with antihypertensive therapy is not recommended, with the exceptions:</p> <ul style="list-style-type: none"> <li>• In patients with acute ischaemic stroke who are eligible for i.v. thrombolysis, <a href="#">BP</a> should be carefully lowered and maintained to &lt;180/105 mmHg for at least the first 24 h after thrombolysis.</li> <li>• In patients with markedly elevated <a href="#">BP</a> who do not receive fibrinolysis, drug therapy may be considered, based on clinical judgement, to reduce <a href="#">BP</a> by 15% during the first 24 h after the stroke onset.</li> </ul>	III	A
	IIa	B
	IIb	C
<p>In hypertensive patients with an acute cerebrovascular event, antihypertensive treatment is recommended:</p> <ul style="list-style-type: none"> <li>• Immediately for <a href="#">TIA</a>.</li> <li>• After several days in ischaemic stroke.</li> </ul>	I	A
	I	A
<p>In all hypertensive patients with ischaemic stroke or <a href="#">TIA</a>, a <a href="#">SBP</a> target range of 120–130 mmHg should be considered.</p>	IIa	B
<p>The recommended antihypertensive drug treatment strategy for stroke prevention is a <a href="#">RAS</a> blocker plus a <a href="#">CCB</a> or a thiazide-like diuretic.</p>	I	A

BP = blood pressure; CCB = calcium-channel blocker; i.v. = intravenous; RAS = renin–angiotensin system; SBP = systolic blood pressure; TIA = transient ischaemic attack.

<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.

Therapeutic strategies in hypertensive patients with Atrial Fibrillation

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In patients with AF, screening for hypertension is recommended.	I	C
A beta-blocker or non-dihydropyridine <a href="#">CCB</a> should be considered as part of the treatment of hypertension if rate control is needed.	IIa	B
Stroke prevention with oral anticoagulation is recommended in patients with AF and hypertension and a <a href="#">CHA2DS2-VASc</a> score of ≥2 in men and ≥3 in women.	I	A
Stroke prevention with oral anticoagulants should be considered in AF patients with hypertension, even when hypertension is the single additional risk factor ( <a href="#">CHA2DS2-VASc</a> score of 1).	IIa	B
Oral anticoagulants should be used with caution in patients with marked <a href="#">BP</a> elevation ( <a href="#">SBP</a> ≥180 mmHg and/or <a href="#">DBP</a> ≥100 mmHg) and the aim should be to lower <a href="#">SBP</a> to at least <140 mmHg and <a href="#">SBP</a> lowering to <130 should be considered. If this is not possible, then patients should make an informed decision that they accept that the stroke protection provided by the anticoagulant will be associated with higher bleeding risk.	IIa	B

AF = atrial fibrillation; BP = blood pressure; CCB = calcium-channel blocker; CHA<sub>2</sub>DS<sub>2</sub>-VASc = Congestive heart failure, Hypertension, Age ≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65–74 years, Sex category (female); DBP = diastolic blood pressure; SBP = systolic blood pressure.

<sup>a</sup>Class of recommendation - <sup>b</sup>Level of evidence.



# Therapeutic strategies in hypertensive patients with Lower Extremity Arterial Disease

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
BP-lowering treatment is recommended to reduce <u>CV</u> risk.	I	A
A combination of an <u>RAS</u> blocker, <u>CCB</u> , or diuretic should be considered as initial therapy.	IIa	B
Beta-blockers may also be considered.	IIb	C

BP = blood pressure; CCB = calcium-channel blocker; CV = cardiovascular; LEAD = lower extremity arterial disease; RAS = renin–angiotensin system. <sup>a</sup>Class of recommendation - <sup>b</sup> Level of evidence.

Many patients with hypertension will be at sufficiently increased [CV](#) risk to be considered for additional treatment strategies to reduce their [CV](#) risk, especially statins and anti-platelet therapy.

Treatment of [CV](#) risk factors associated with hypertension

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<a href="#">CV</a> risk assessment with the <a href="#">SCORE</a> system is recommended for hypertensive patients who are not already at high or very risk due to established <a href="#">CVD</a> , renal disease, or diabetes.	I	B
For patients at very high <a href="#">CV</a> risk, statins are recommended to achieve <a href="#">LDL-C</a> levels of <1.8 mmol/L (70 mg/dL), or a reduction of ≥50% if the baseline <a href="#">LDL-C</a> is 1.8–3.5 mmol/L (70–135 mg/dL).	I	B
For patients at high <a href="#">CV</a> risk, statins are recommended to achieve an <a href="#">LDL-C</a> goal of <2.6 mmol/L (100 mg/dL) or a reduction of ≥50% if the baseline <a href="#">LDL-C</a> is 2.6–5.2 mmol/L (100–200 mg/dL).	I	B
For patients at low-moderate <a href="#">CV</a> risk, statins should be considered, to achieve an <a href="#">LDL-C</a> value of <3.0 mmol/L (115 mg/dL).	IIa	C
Antiplatelet therapy, in particular low-dose aspirin, is recommended for secondary prevention in hypertensive patients.	I	A
Aspirin is not recommended for primary prevention in hypertensive patients without <a href="#">CVD</a> .	III	A

CV = cardiovascular; CVD = cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; SCORE = Systematic COronary Risk Evaluation.

<sup>a</sup>Class of recommendation - <sup>b</sup> Level of evidence.



After the initiation of antihypertensive drug therapy, the patient should be reviewed to evaluate the [BP](#) control and assess possible adverse effects of treatment. [SPC](#) therapy should reduce [BP](#) within 1–2 weeks and may continue to reduce [BP](#) over the next 2 months. The initial review should be within the first 2 months and the frequency of review will depend on the severity of hypertension, the urgency to achieve [BP](#) control, and the patient’s comorbidities. Once the [BP](#) target is reached, the review visit interval will depend on the need to monitor comorbidities or renal function and will range from 3 to 12 months. Strategies that may help increase adherence to treatment are shown in [table 27](#). These are especially important in patients whose [BP](#) is not controlled.

According to local policies and the availability of local health resources, many of the later visits may be performed by nurses or other non-physician health workers. For stable patients, [HBPM](#) and electronic communication with the physician may provide an alternative to reduce the frequency of visits. It is advisable to assess risk factors and asymptomatic organ damage at least every 2 years.

**Table 27 Interventions that may improve drug adherence in hypertension**

**Physician level**

Provide information on the risks of hypertension and the benefits of treatment, as well as agreeing a treatment strategy to achieve and maintain [BP](#) control using lifestyle measures and a single-pill–based treatment strategy when possible (information material, programmed learning, computer-aided counselling)

Empowerment of the patient

Feedback on behavioural and clinical improvements

Assessment and resolution of individual barriers to adherence



Collaboration with other healthcare providers, especially nurses and pharmacists

## Patient level

Self-monitoring of [BP](#) (including telemonitoring)

Group sessions

Instruction combined with motivational strategies

Self-management with simple patient-guided systems

Use of reminders

Obtain family, social, or nurse support

Provision of drugs at worksite

## Drug-treatment level

Simplification of the drug regimen favouring the use of [SPC](#) therapy

Reminder packaging

## Health-system level

Support the development of monitoring systems (telephone follow-up, home visits, telemonitoring of home BP)

Support financially the collaboration between healthcare providers (pharmacists, nurses)

Reimbursement of [SPC](#) pills

Development of national databases, including prescription data, available for physicians and pharmacists

Accessibility to drugs

BP = blood pressure; SPC = single-pill combination.

